Supporting Information

Synthesis of a New Family of Acyclic Nucleoside Phosphonates, Analogues of TPases Transition States

Bénédicte Dayde,[a,b] Samira Benzaria,[b] Claire Pierra,[b] Gilles Gosselin,[b,c]
Dominique Surleraux,[b] Jean-Noel Volle,[a] Jean-Luc Pirat,[a] David Virieux[a,*]

[a] *AM2N, Institut Charles Gerhardt, UMR 5253, ENSCM, 8, rue de l'Ecole Normale, F-34296 Montpellier – France. Fax: +33 (0)467 14 43 19; Tel: +33 (0)467 14 43 14; E-mail:david.virieux@enscm.fr*
[b] *Idenix Pharmaceuticals, Medicinal Chemistry Laboratory, Cap Gamma, 1682 rue de la Valsière, BP50001, 34189 Montpellier Cedex 4 – France.*
[c] *UMR5247 CNRS-UM1-UM2 (IBMM), Université Montpellier 2, 34095 Montpellier Cedex 5, France.*
david.virieux@enscm.fr

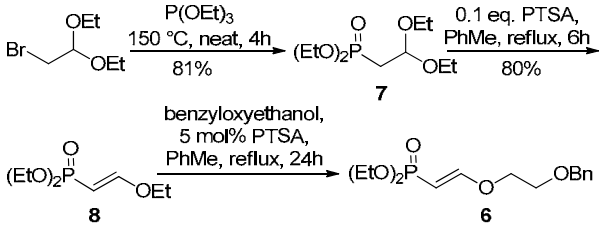
Table of contents

I. General Considerations

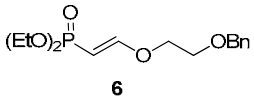
Before use, commercial reagents were purified by distillation or sublimation. All manipulations were carried out using standard Schlenck Techniques. Solvents were dried according to current methods, distilled and stored under nitrogen atmosphere. All reactions involving air or moisture sensitive reagents or intermediates were carried out under dry nitrogen in flame-dried glassware. Melting points were measured on a Büchi B-540 apparatus and are uncorrected. All new compounds were characterized by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR using a Bruker DRX 400 MHz NMR spectrometer or a Bruker Avance 250 MHz NMR spectrometer. All NMR experiments performed on phosphorus were indicated uncoupling of hydrogen. All NMR led during reaction were done with a closed capillary DMSO-D6 probe in the NMR tube. Low and high resolution mass spectra were determined on an electrospray ionization (RSI) WATERS Micromas Q-Tof spectrometer with as internal reference H3PO4 (0.1% in water/acetonitrile, 1:1).

II. NMR and mass spectra

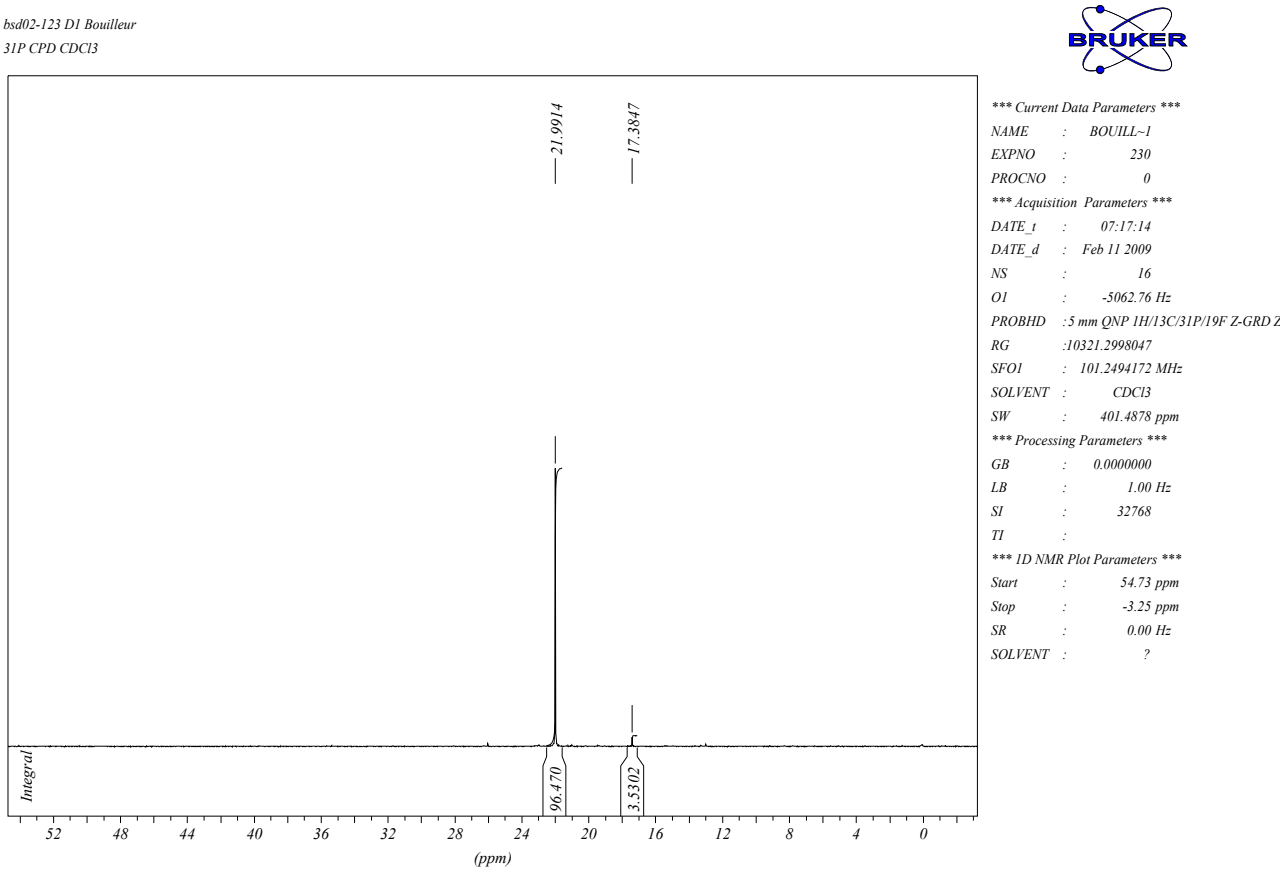
II.1. *(E)*-diethyl 2-[2-(benzyloxy)ethoxy]vinylphosphonate 6



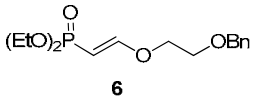
Scheme 1 Synthesis of benzyloxyethyloxyethylenylphosphonate **6**



$C_{15}H_{23}O_5P$
MW = 314.32 g.mol^{-1}
Yellow oil (9.09 g, 79%)

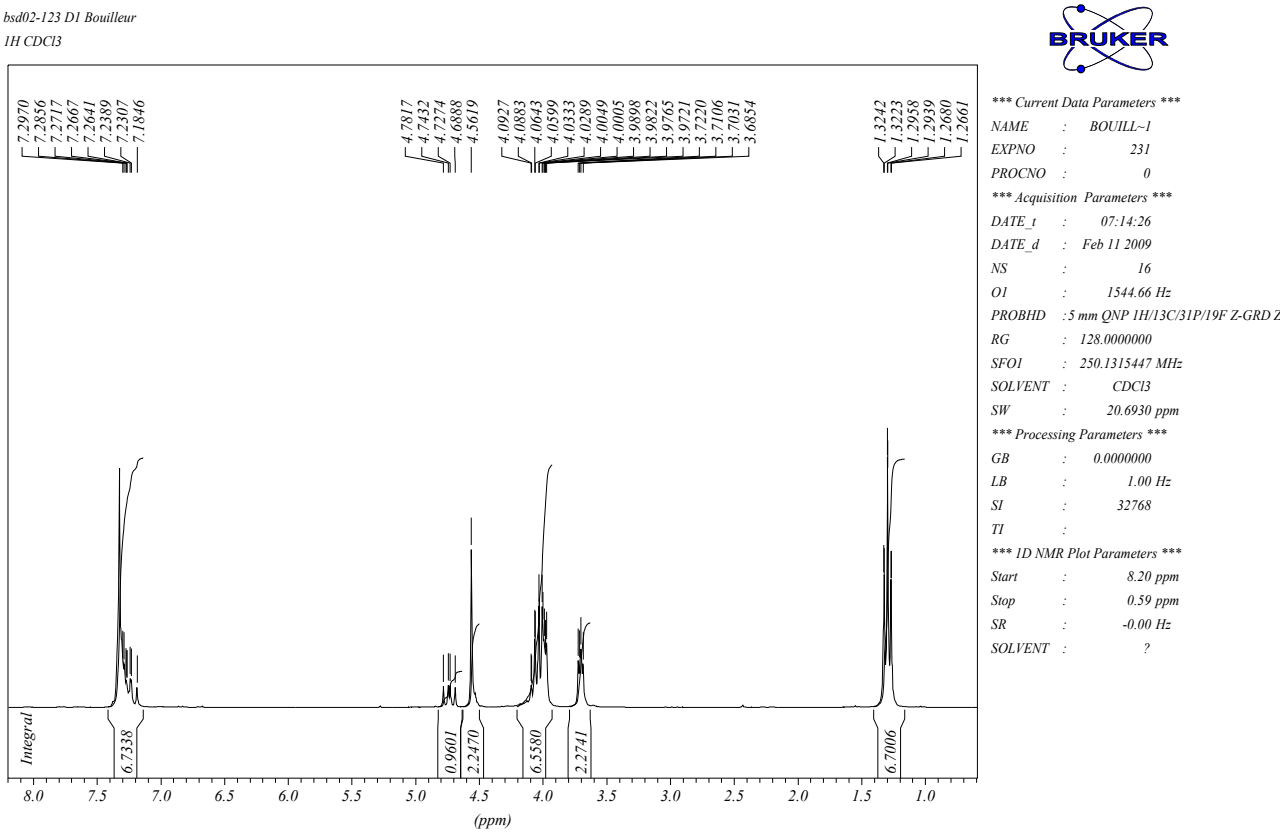


(E)-diethyl 2-[2-(benzyloxy)ethoxy]vinylphosphonate 6



6

$C_{15}H_{23}O_5P$
MW = 314.32 g.mol^{-1}
Yellow oil (9.09 g, 79%, instable to storage)



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DATE_d : Feb 11 2009
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RG : 128.0000000
SFO1 : 250.1315447 MHz
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SW : 20.6930 ppm
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LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
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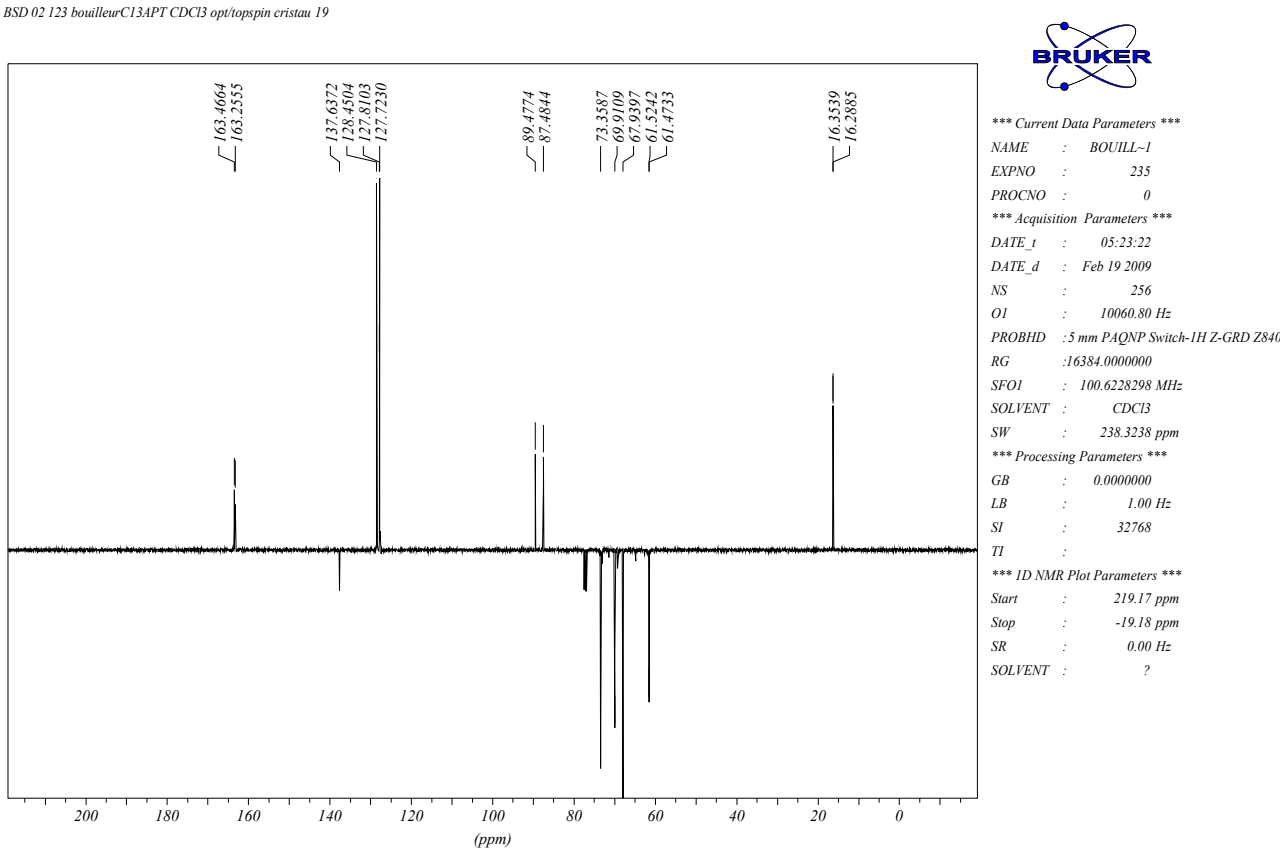
Stop : 0.59 ppm
SR : -0.00 Hz
SOLVENT : ?



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PROCNO : 0
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DATE_d : Feb 19 2009
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O1 : 10060.80 Hz
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RG : 16384.0000000
SFO1 : 100.6228298 MHz
SOLVENT : CDCl3
SW : 238.3238 ppm
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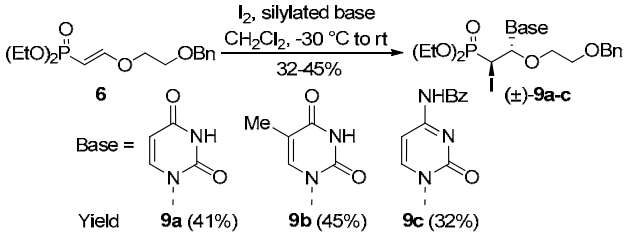
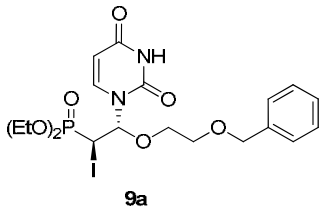
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 219.17 ppm
Stop : -19.18 ppm
SR : 0.00 Hz
SOLVENT : ?

II.2. *(±)*-(*1R,2R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-1-iodoethylphosphonate 9a

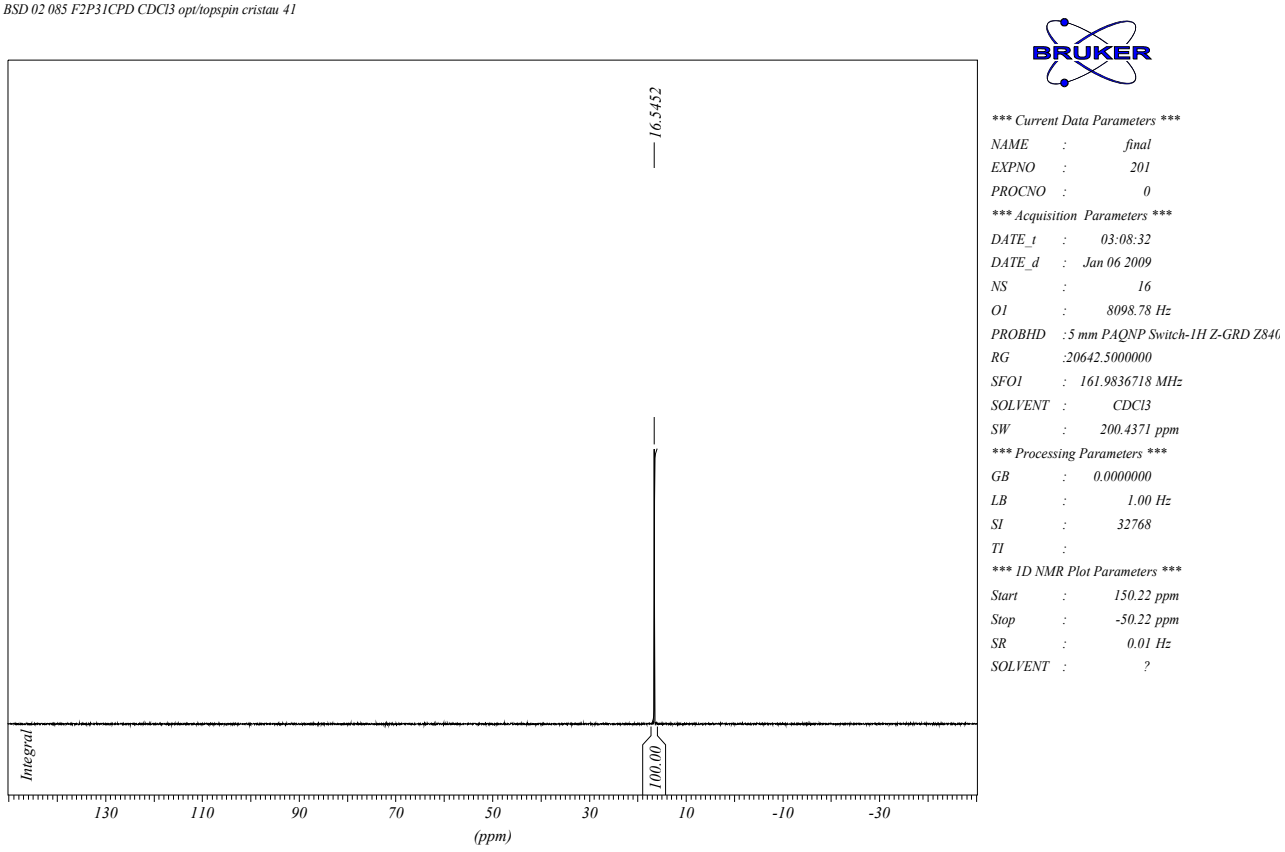


Scheme 2 Iodo-base introduction on **6**

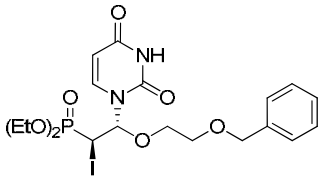


$C_{19}H_{26}IN_2O_7P$
MW = 552.31 g.mol^{-1}
Colorless oil (0.35 g, 40 %)

BSD 02 085 F2P31CPD CDCl3 opt/topspin cristau 41



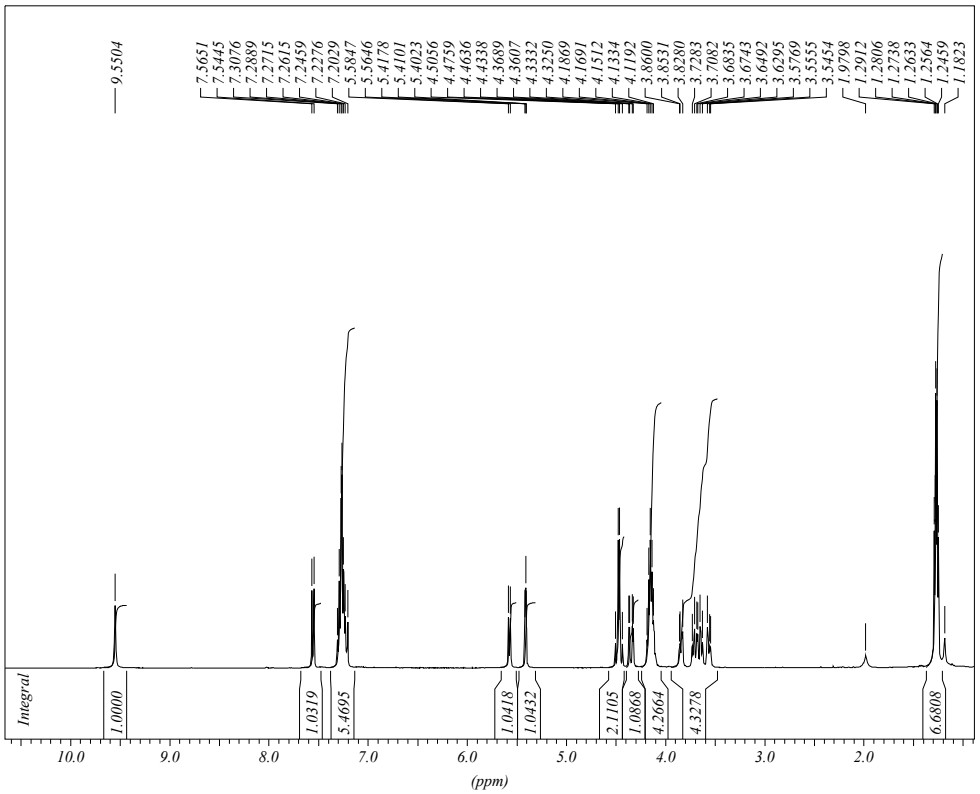
(±)-(*1R,2R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-1-iodoethylphosphonate 9a



9a

$C_{19}H_{26}IN_2O_7P$
MW = 552.31 g.mol^{-1}
Colorless oil (0.35 g, 40 %)

BSD 02 085 F2PROTON CDCl3 opt/topspin cristau 41



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DATE_d : Jan 06 2009
NS : 16
O1 : 2400.78 Hz
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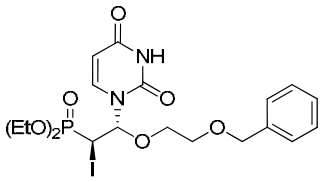
RG : 71.8000031
SFO1 : 400.1324008 MHz
SOLVENT : CDCl3
SW : 14.9831 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 10.66 ppm
Stop : 0.89 ppm
SR : 32.79 Hz
SOLVENT : ?

(±)-(*1R,2R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-1-iodoethylphosphonate 9a



9a

$C_{19}H_{26}IN_2O_7P$
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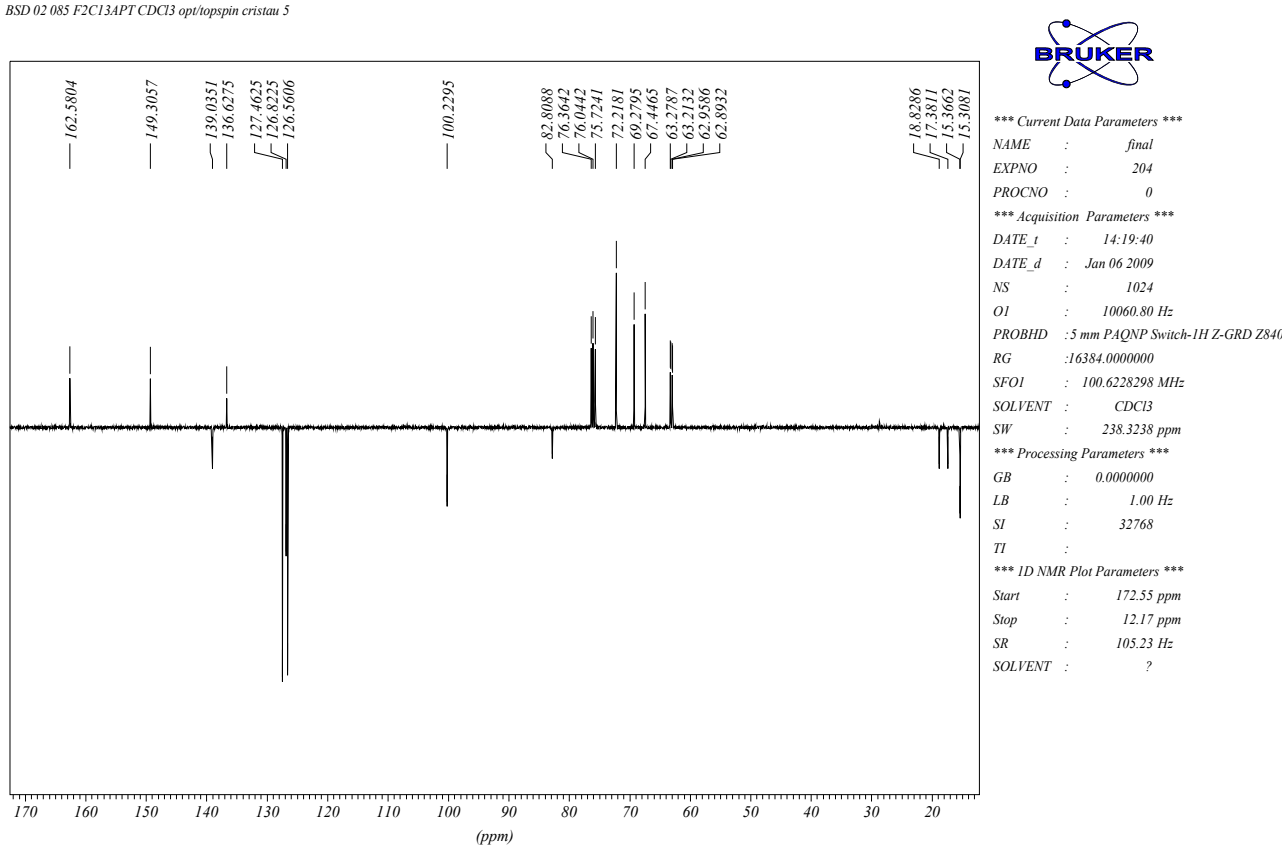
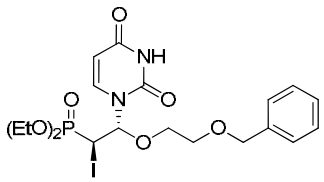


(±)-(*1R,2R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-1-iodoethylphosphonate 9a



9a

$C_{19}H_{26}IN_2O_7P$
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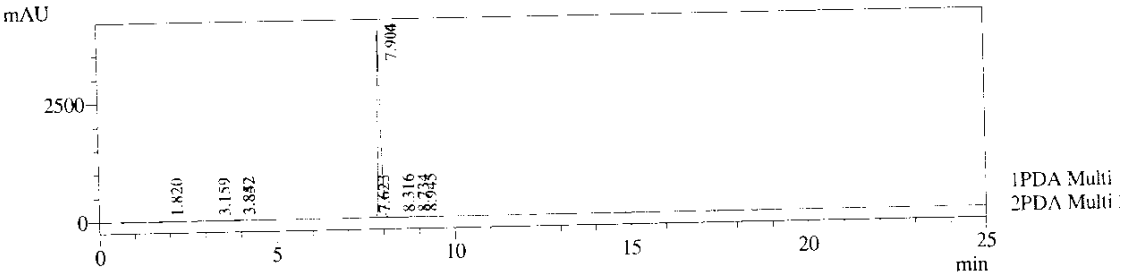
Colorless oil (0.35 g, 40 %)

==== Shimadzu LCsolution Analysis Report ====

C:\...\BSD 02 085 Final gradient10-95 10µL.lcd

Acquired by	: Admin
Sample Name	: BSD02085
Sample ID	: BSD02085
Tray#	: 1
Vail #	: 31
Injection Volume	: 10 uL
Data File Name	: BSD 02 085 Final gradie
Method File Name	: Methode Pierre 2.lcm
Batch File Name	: 06-01-09 grad10-95-2.lc
Report File Name	: bene report.lcr
Data Acquired	: 06/01/2009 17:27:06
Data Processed	: 06/01/2009 18:29:01

Chromatogram
BSD02085 C:\LabSolutions\Data\Project1\Bénédicte\BSD 02 085 Final gradient10-95 10µL.lcd



1 PDA Multi 1 / 254nm 4nm
2 PDA Multi 2 / 213nm 4nm

Chromatogram
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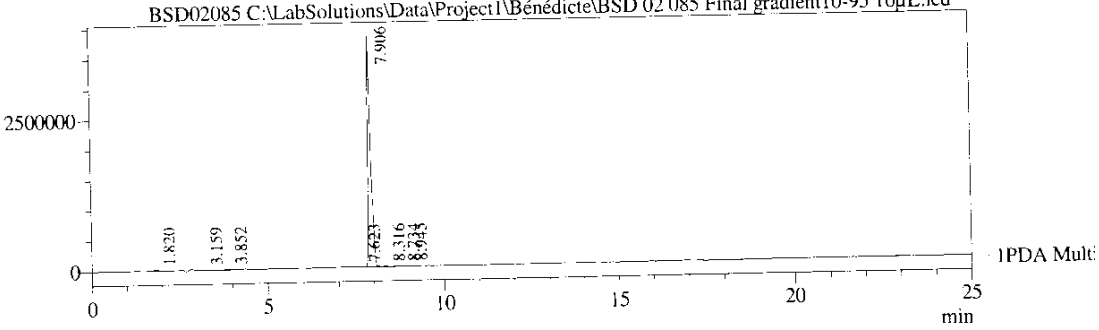


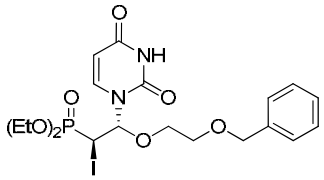
1 PDA Multi 2 / 213nm 4nm

PeakTable

PDA Ch2 213nm 4nm

Pic	Temps ret.	Hauteur	Aire	Hauteur %	Aire %
1	1.820	13146	196061	0.337	0.874
2	3.159	7932	86657	0.204	0.387
3	3.852	17314	211932	0.444	0.945
4	7.623	5226	28874	0.134	0.129
5	7.906	3828054	21705216	98.243	96.808
6	8.316	8326	68701	0.214	0.306
7	8.734	5377	56009	0.138	0.250
8	8.945	11134	67396	0.286	0.301
Total		3896508	22420846	100.000	100.000

***(±)*-(*1R,2R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-1-iodoethylphosphonate 9a**



9a

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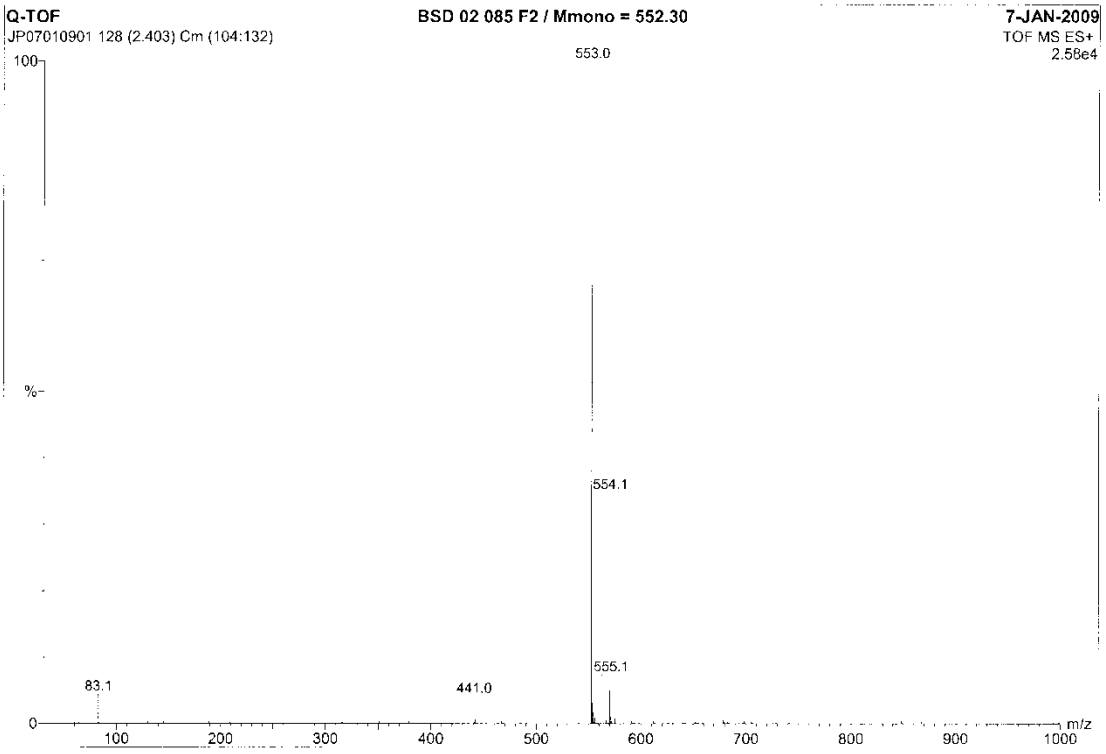
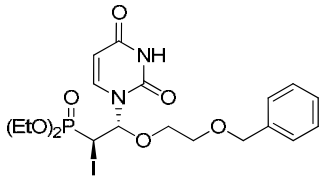


***(±)*-(*1R,2R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-1-iodoethylphosphonate 9a**



9a

$C_{19}H_{26}IN_2O_7P$
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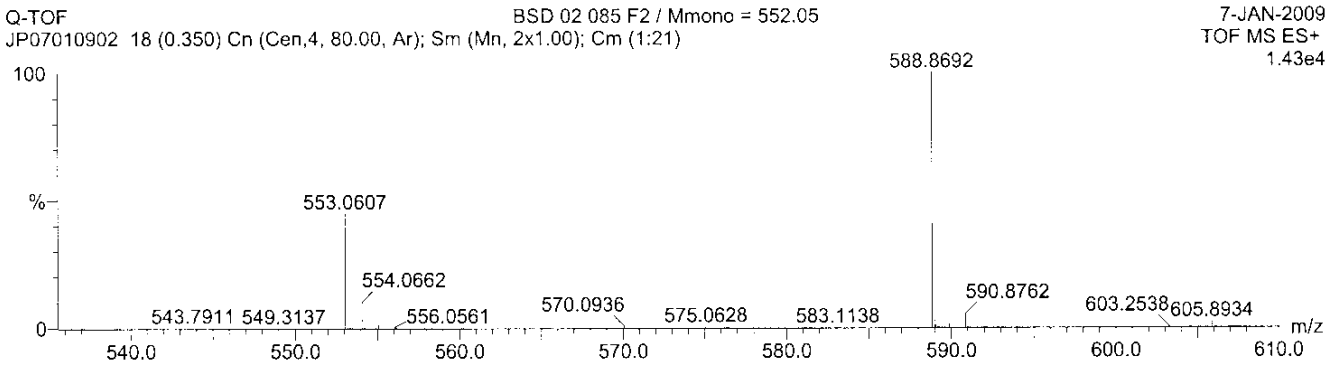
Colorless oil (0.35 g, 40 %)

Elemental Composition Report Page 1

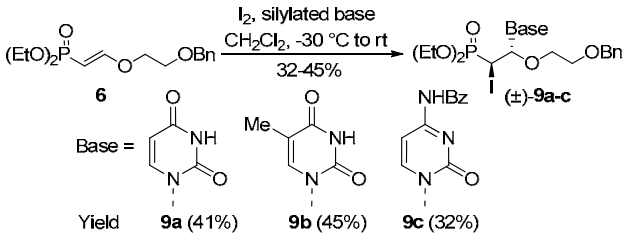
Single Mass Analysis
Tolerance = 3.0 mDa / DBE: min = -5.0, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
50 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)

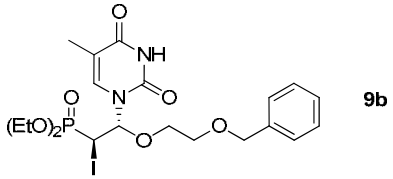


Minimum:				-5.0		
Maximum:		3.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
553.0607	553.0601	0.6	1.1	7.5	1	C19 H27 N2 O7 P I
	553.0587	2.0	3.6	8.0	2	C17 H25 N5 O6 P I

II.3. (±)-(1*R*,2*R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-1-iodoethylphosphonate 9b

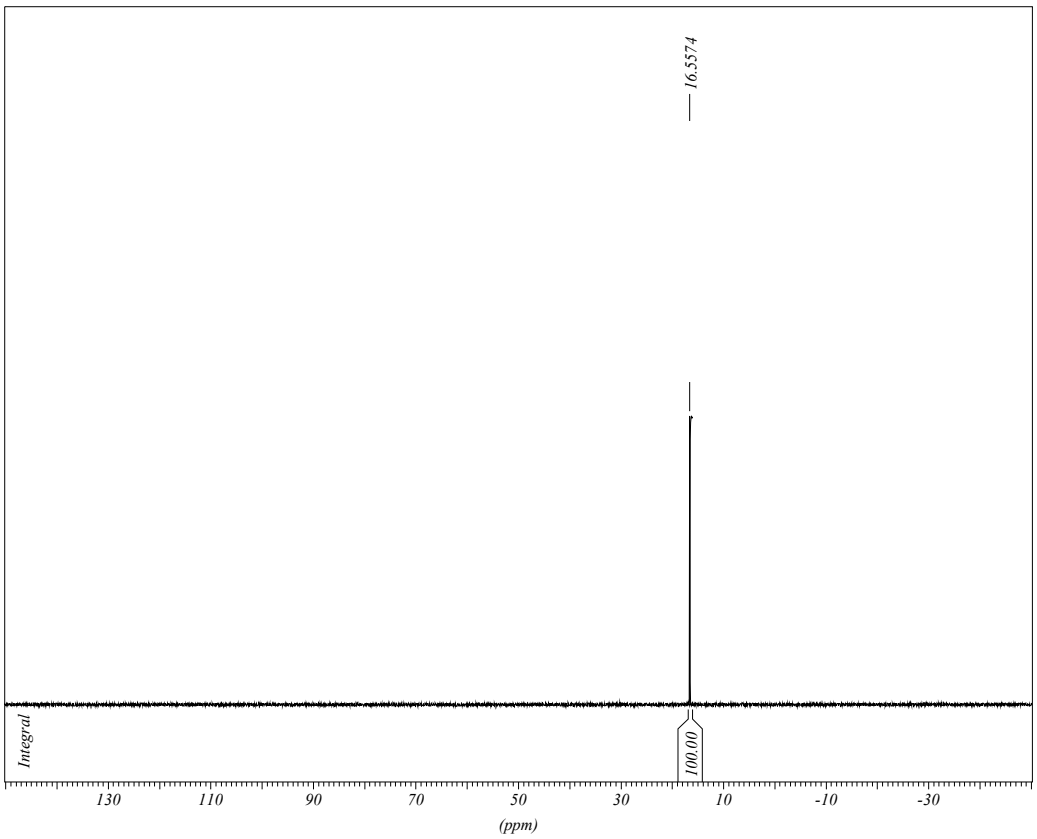


Scheme 2 Iodo-base introduction on **6**



$C_{20}H_{28}IN_2O_7P$
MW = 566.33 g.mol^{-1}
Colorless oil (0.81 g, 45 %)

BSD 02 099 F3P31CPD CDCl3 opt/topspin cristau 35



BRUKER

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PROCNO : 0
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DATE_d : Jan 20 2009
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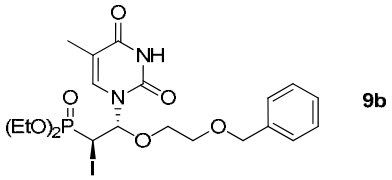
NUC1 : 31P
O1 : 8098.78 Hz
O2 : 1600.52 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG :20642.5000000
SFO1 : 161.9836718 MHz
SW : 200.4371 ppm
SW_h : 32467.532 Hz
TD : 65536
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
PC : 1.40
SF : 161.9755730 MHz
*** 1D NMR Plot Parameters ***
Start : 150.22 ppm
Stop : -50.22 ppm
SR : 0.01 Hz
ppm_cm : 9.46
Hz_cm : 1531.49

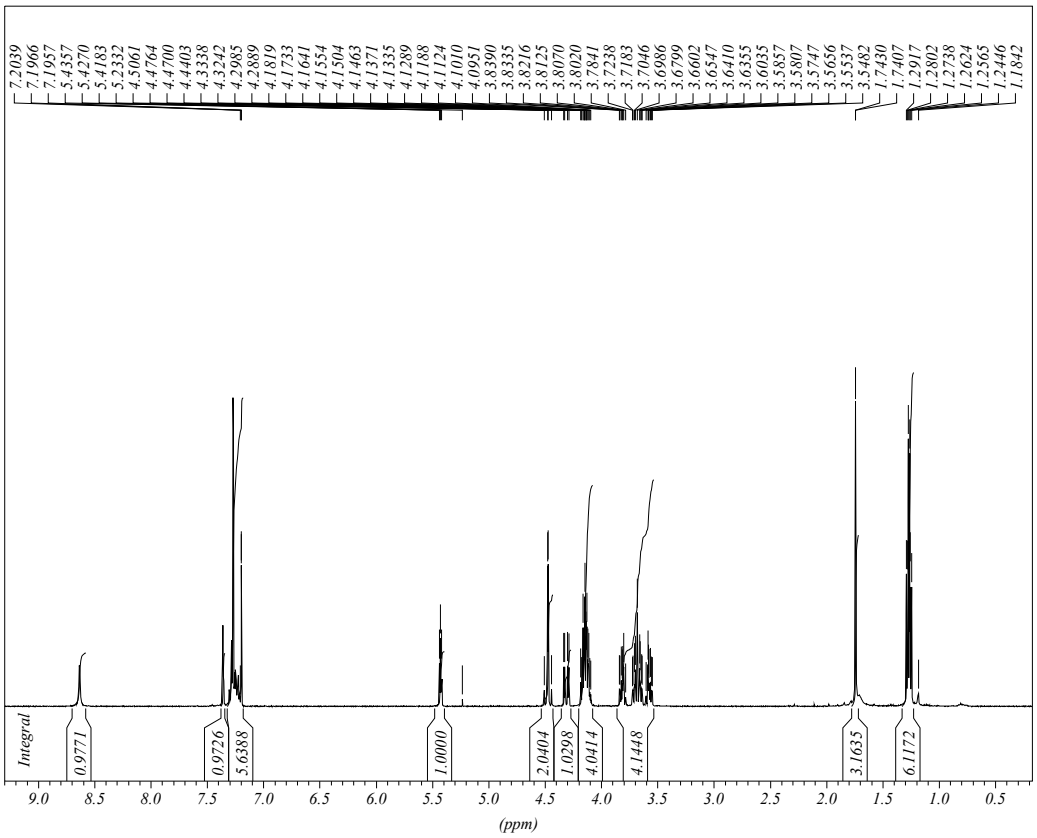
(±)-(1*R*,2*R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-1-iodoethylphosphonate 9b



9b

$C_{20}H_{28}IN_2O_7P$
MW = 566.33 g.mol^{-1}
Colorless oil (0.81 g, 45 %)

BSD 02 099 F3PROTON CDCl3 opt/topspin cristau 38



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PROCNO : 0
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DATE_d : Jan 27 2009
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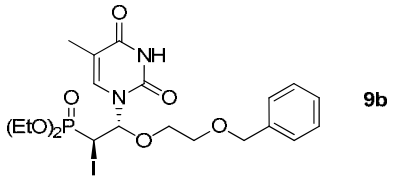
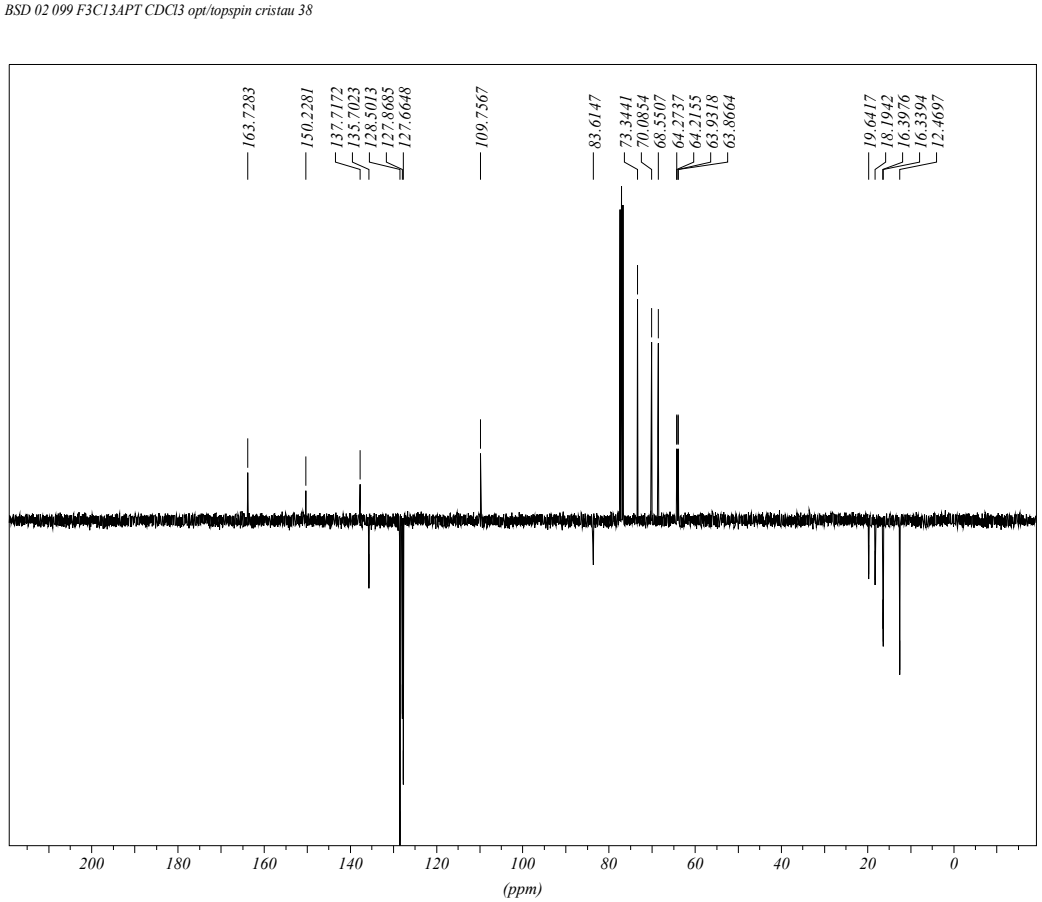
DS : 2
NS : 16
NUC1 : 1H
O1 : 2400.78 Hz
O2 : 2470.97 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-GRD Z840
RG : 143.6999969
SFO1 : 400.1324008 MHz
SW : 14.9831 ppm
SW_h : 5995.204 Hz
TD : 65536
*** Processing Parameters ***
GB : 0.0000000
LB : 0.10 Hz
PC : 1.00
SF : 400.1300353 MHz
*** 1D NMR Plot Parameters ***
Start : 9.30 ppm
Stop : 0.17 ppm
SR : 35.32 Hz
ppm_cm : 0.43
Hz_cm : 172.27

(±)-(1*R*,2*R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-1-iodoethylphosphonate 9b

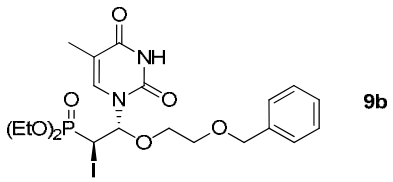


9b

$C_{20}H_{28}IN_2O_7P$
MW = 566.33 g.mol^{-1}
Colorless oil (0.81 g, 45 %)



(±)-(1*R*,2*R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-1-iodoethylphosphonate 9b



9b

$C_{20}H_{28}IN_2O_7P$
MW = 566.33 g.mol^{-1}
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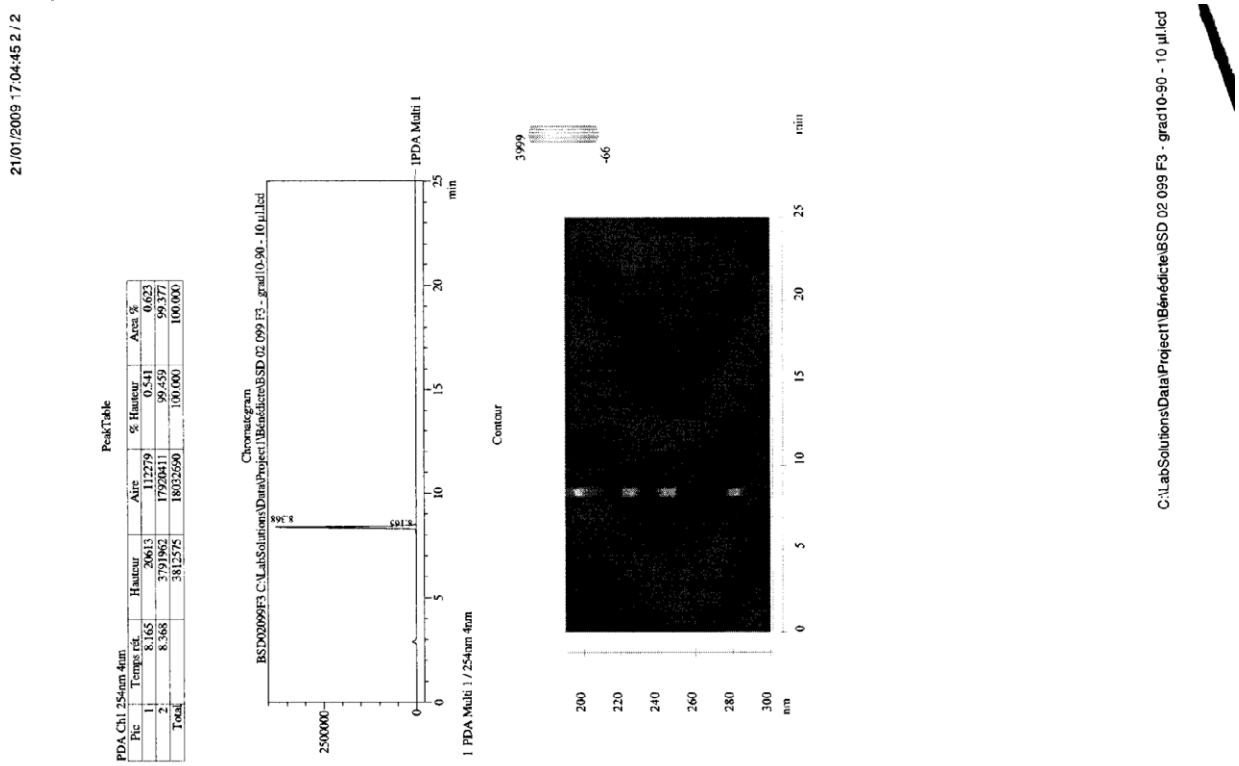
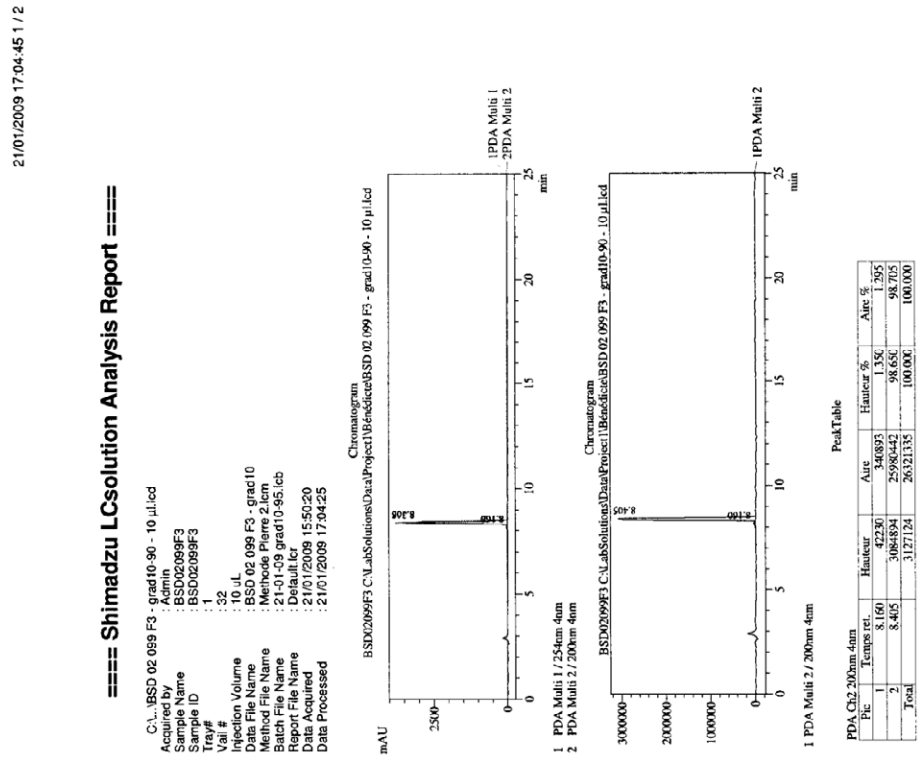
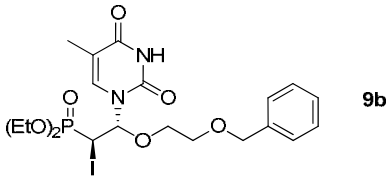




(±)-(1*R*,2*R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-1-iodoethylphosphonate 9b



9b

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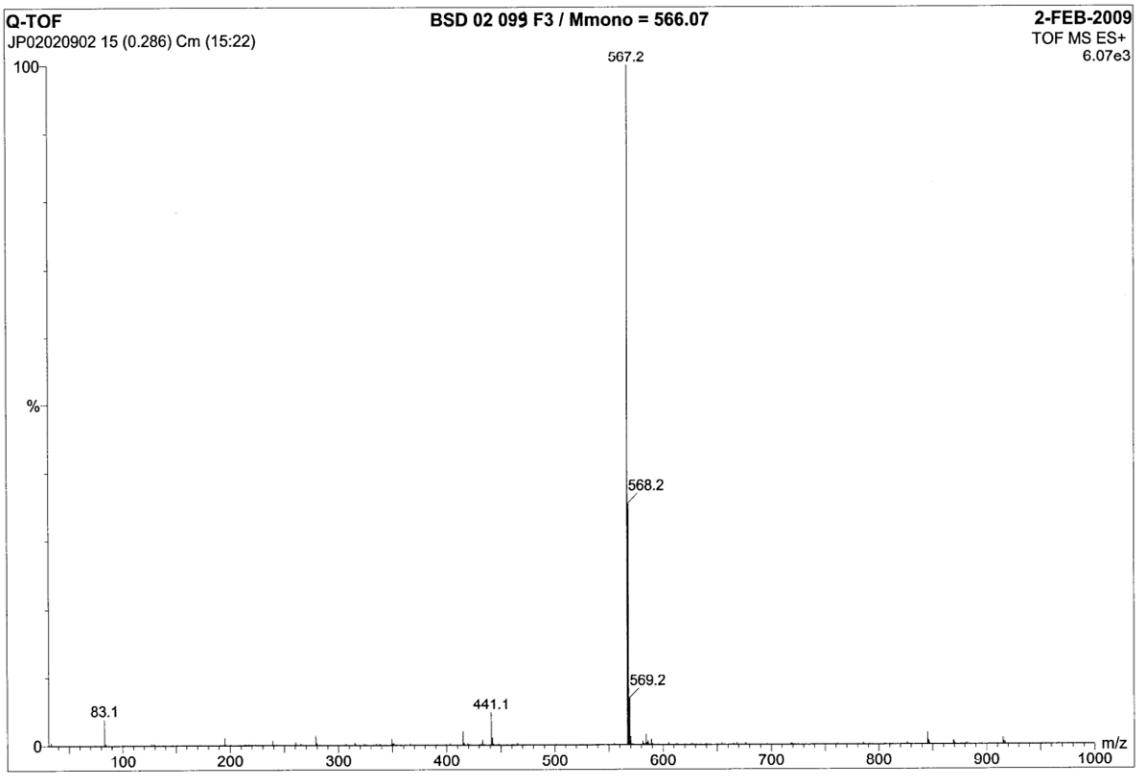
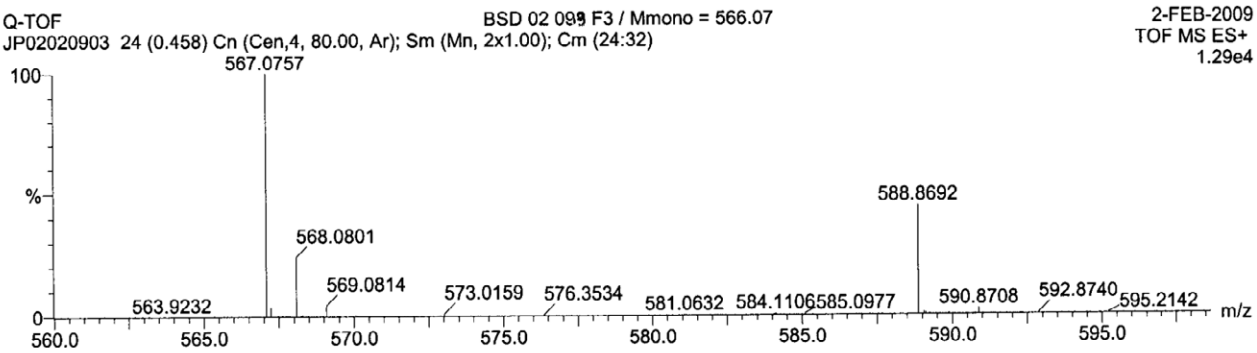


Elemental Composition Report

Page 1

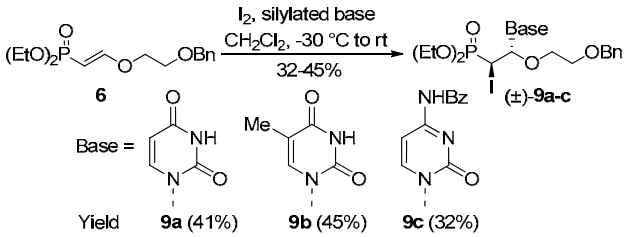
Single Mass Analysis
Tolerance = 4.0 mDa / DBE: min = -5.0, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
136 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

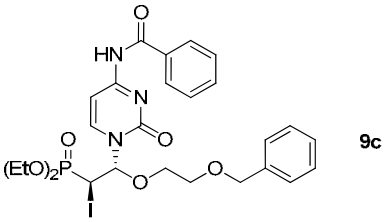


Minimum:				-5.0		
Maximum:		4.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
567.0757	567.0757	0.0	0.0	7.5	1	C20 H29 N2 O7 P I
	567.0744	1.3	2.3	8.0	2	C18 H27 N5 O6 P I
	567.0730	2.7	4.7	3.0	3	C17 H31 N O10 P I

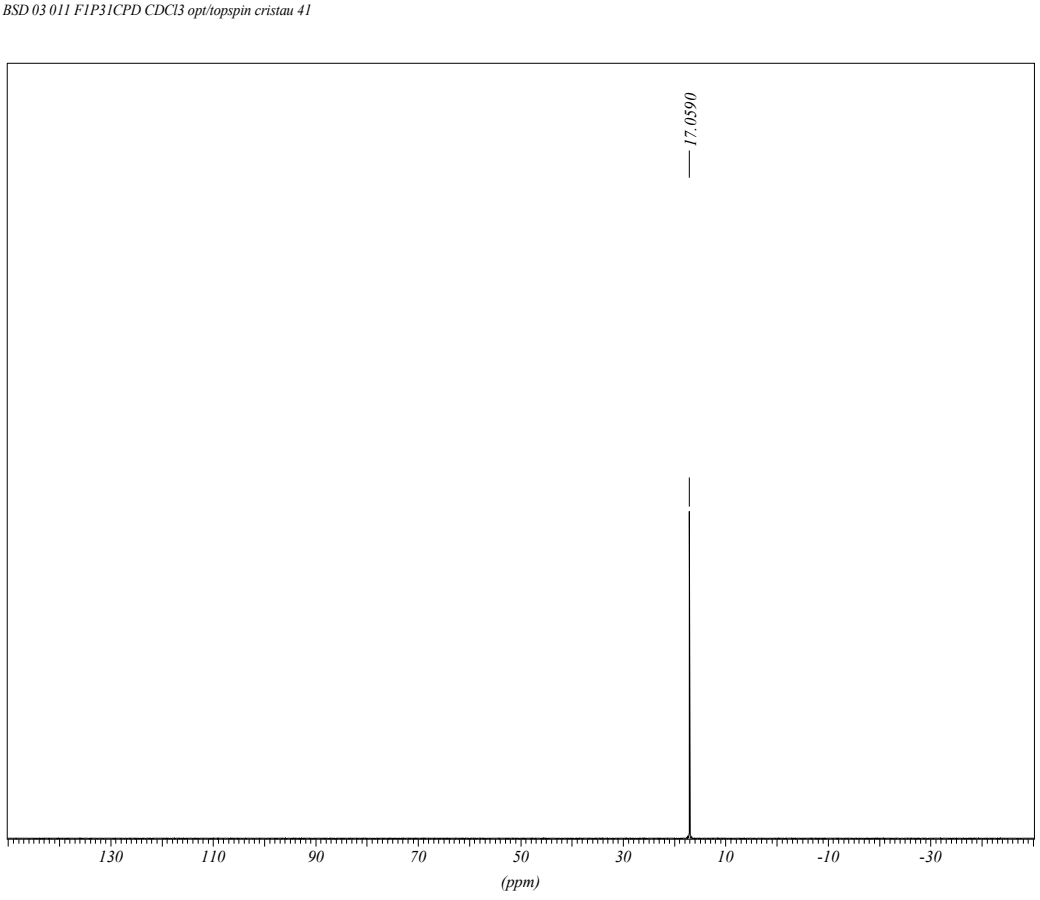
II.4. (±)-(1*R*,2*R*)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-[2-(4-benzoylamino-2-oxo-2H-pyrimidin-1-yl)]-1-iodoethylphosphonate 9c

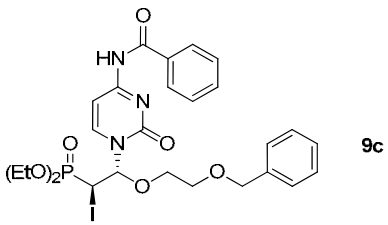


Scheme 2 Iodo-base introduction on **6**



$C_{26}H_{31}N_3O_7IP$
MW = 655.43 g.mol^{-1}
White solid (620 mg, 32 %)

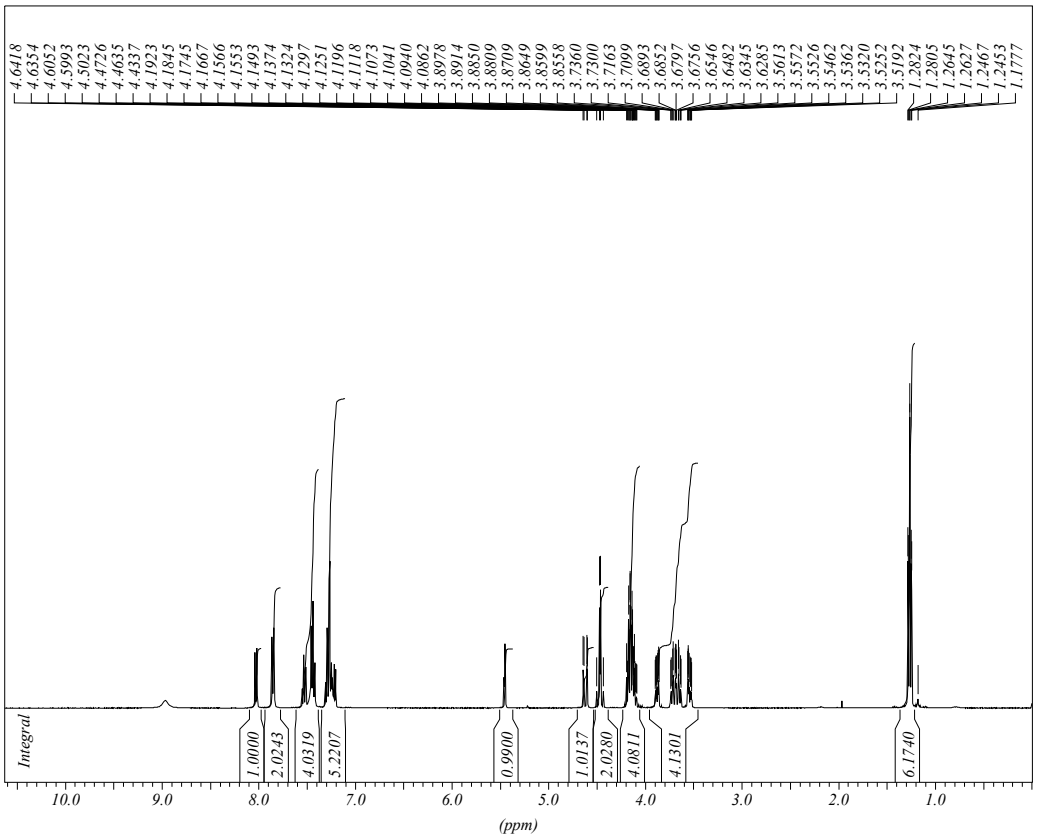




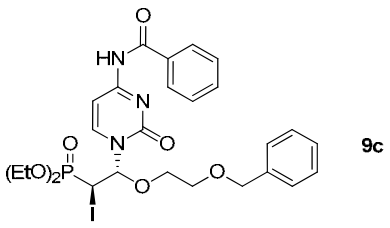
9c

$C_{26}H_{31}N_3O_7IP$
MW = 655.43 g.mol^{-1}
White solid (620 mg, 32 %)

BSD 03 011 F1+F2PROTON CDCl3 opt/topspin cristau 59



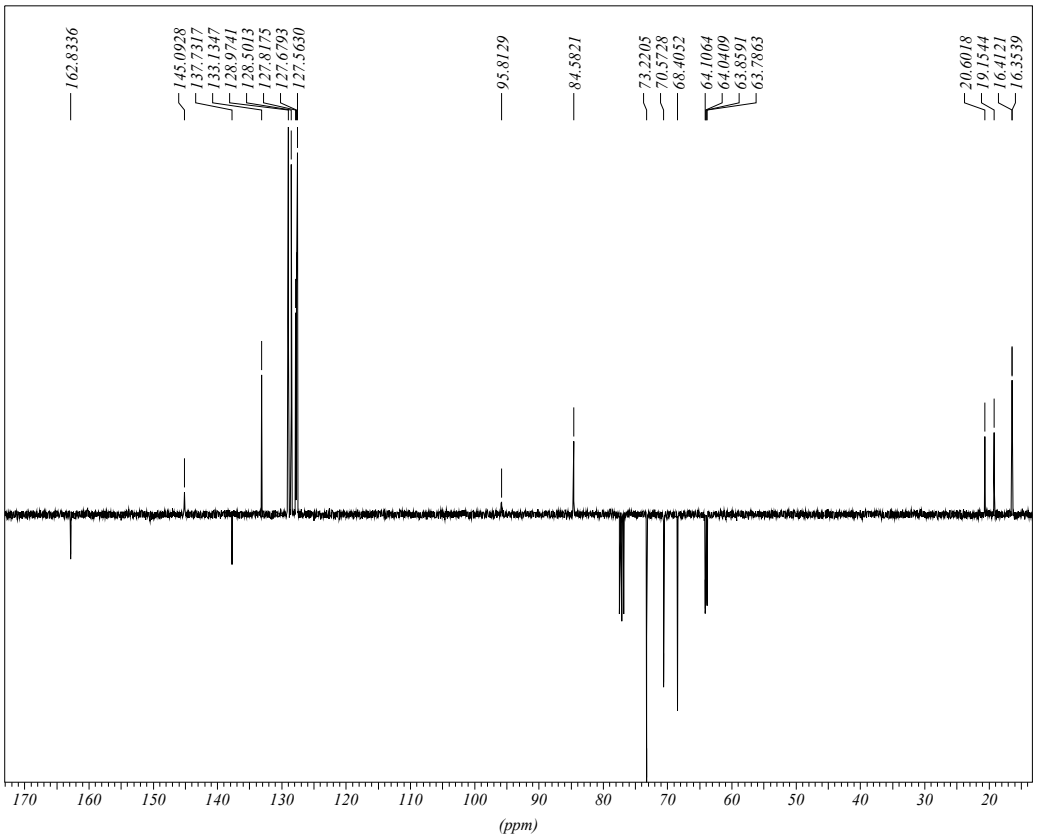
*** Current Data Parameters ***
NAME : pursec
EXPNO : 202
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 00:32:36
DATE_d : Mar 20 2009
DE : 6.0 usec
DS : 2
NS : 16
NUC1 : 1H
O1 : 2400.78 Hz
O2 : 2470.97 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-GRD Z840
RG : 64.0000000
SFO1 : 400.1324008 MHz
SW : 14.9831 ppm
SW_h : 5995.204 Hz
TD : 65536
*** Processing Parameters ***
GB : 0.0000000
LB : 0.10 Hz
PC : 1.00
SF : 400.1300334 MHz
*** 1D NMR Plot Parameters ***
Start : 10.63 ppm
Stop : -0.00 ppm
SR : 33.37 Hz
ppm_cm : 0.50
Hz_cm : 200.69



9c

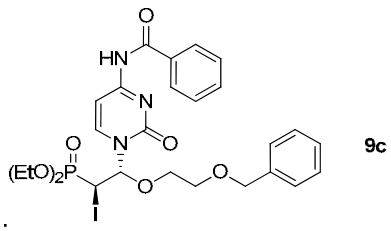
$C_{26}H_{31}N_3O_7IP$
MW = 655.43 g.mol^{-1}
White solid (620 mg, 32 %)

BSD 03 011 F1+F2C13APT CDCl3 opt/topspin cristau 59



BRUKER

*** Current Data Parameters ***
NAME : pursec
EXPNO : 201
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 00:29:26
DATE_d : Mar 20 2009
DE : 6.0 usec
DS : 4
NS : 256
NUC1 : 13C
O1 : 10060.80 Hz
O2 : 1600.52 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG :16384.0000000
SFO1 : 100.6228298 MHz
SW : 238.3238 ppm
SW_h : 23980.815 Hz
TD : 65536
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
PC : 1.40
SF : 100.6127690 MHz
*** 1D NMR Plot Parameters ***
Start : 173.11 ppm
Stop : 13.25 ppm
SR : 0.00 Hz
ppm_cm : 7.54
Hz_cm : 758.69



9c

$C_{26}H_{31}N_3O_7IP$
MW = 655.43 g.mol^{-1}
White solid (620 mg, 32 %)

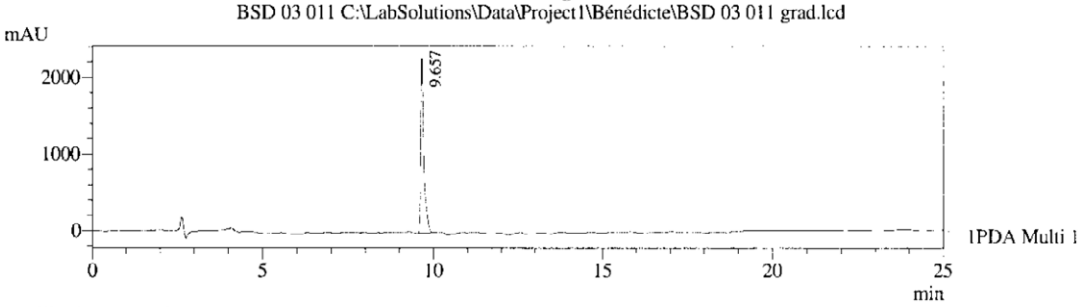
01/04/2009 17:34:17 1

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\Bénédicte\BSD 03 011 grad.lcd

Acquired by	: Admin
Sample Name	: BSD 03 011
Sample ID	: BSD 03 011
Tray#	: 1
Vail #	: 95
Injection Volume	: 10 uL
Data File Name	: BSD 03 011 grad.lcd
Method File Name	: Methode Pierre 2.lcm
Batch File Name	: 01-04-09 grad10-95.lcb
Report File Name	: bene report.lcr
Data Acquired	: 01/04/2009 17:05:28
Data Processed	: 01/04/2009 17:33:48

Chromatogram
BSD 03 011 C:\LabSolutions\Data\Project1\Bénédicte\BSD 03 011 grad.lcd

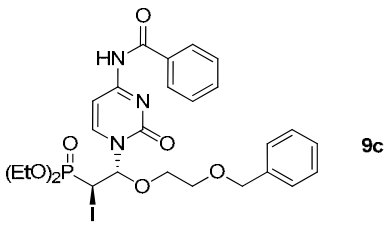


1 PDA Multi 1 / 192nm 4nm

PeakTable

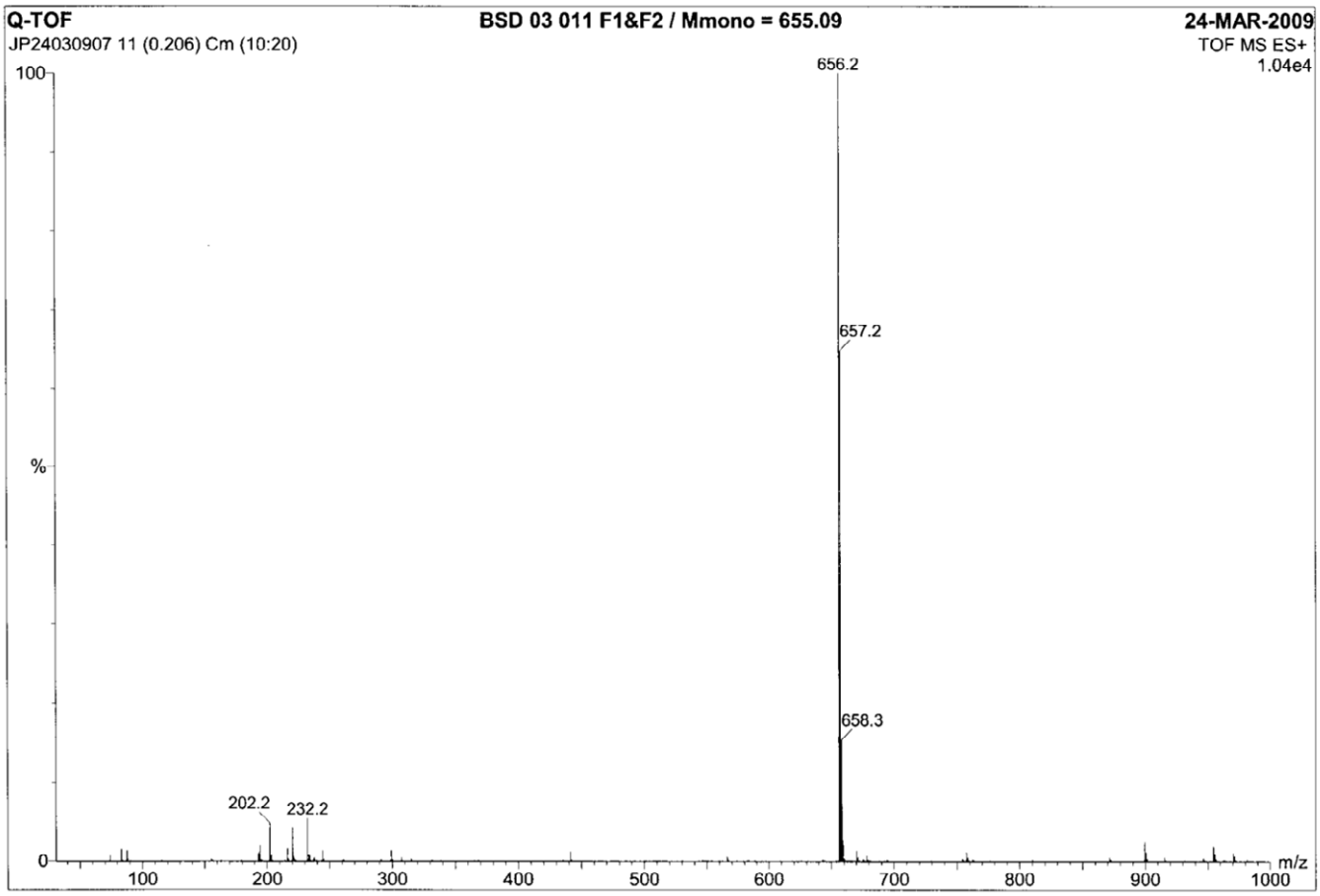
PDA Ch1 192nm 4nm

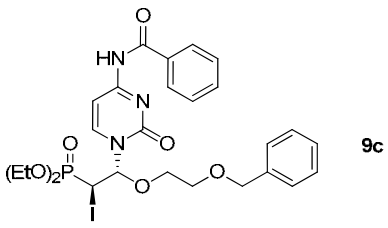
Pic	Temps rét.	Hauteur	Aire	% Hauteur	Area %
1	9.657	2305109	15658804	100.000	100.000
Total		2305109	15658804	100.000	100.000



9c

$C_{26}H_{31}N_3O_7IP$
MW = 655.43 g.mol^{-1}
White solid (620 mg, 32 %)





9c

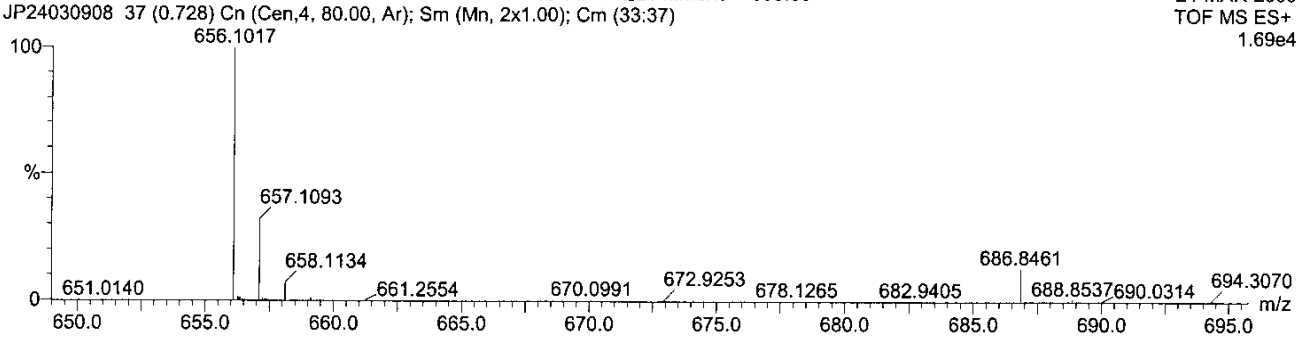
$C_{26}H_{31}N_3O_7IP$
MW = 655.43 g.mol^{-1}
White solid (620 mg, 32 %)

Elemental Composition Report **Page 1**

Single Mass Analysis (displaying only valid results)
Tolerance = 3.0 mDa / DBE: min = -5.0, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

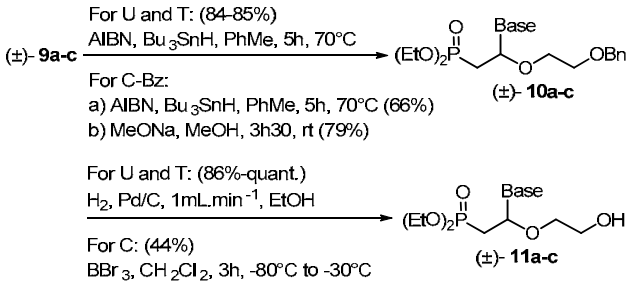
Monoisotopic Mass, Odd and Even Electron Ions
166 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)

Q-TOF BSD 03 011 F1F2 / Mmono = 655.09 24-MAR-2009
JP24030908 37 (0.728) Cn (Cen,4, 80.00, Ar); Sm (Mn, 2x1.00); Cm (33:37) TOF MS ES+
1.69e4

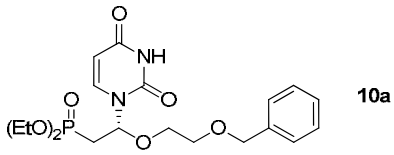


Minimum:				-5.0		
Maximum:		3.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
656.1017	656.1023	-0.6	-0.9	12.5	1	C26 H32 N3 O7 P I
	656.0996	2.1	3.2	8.0	2	C23 H34 N2 O10 P I

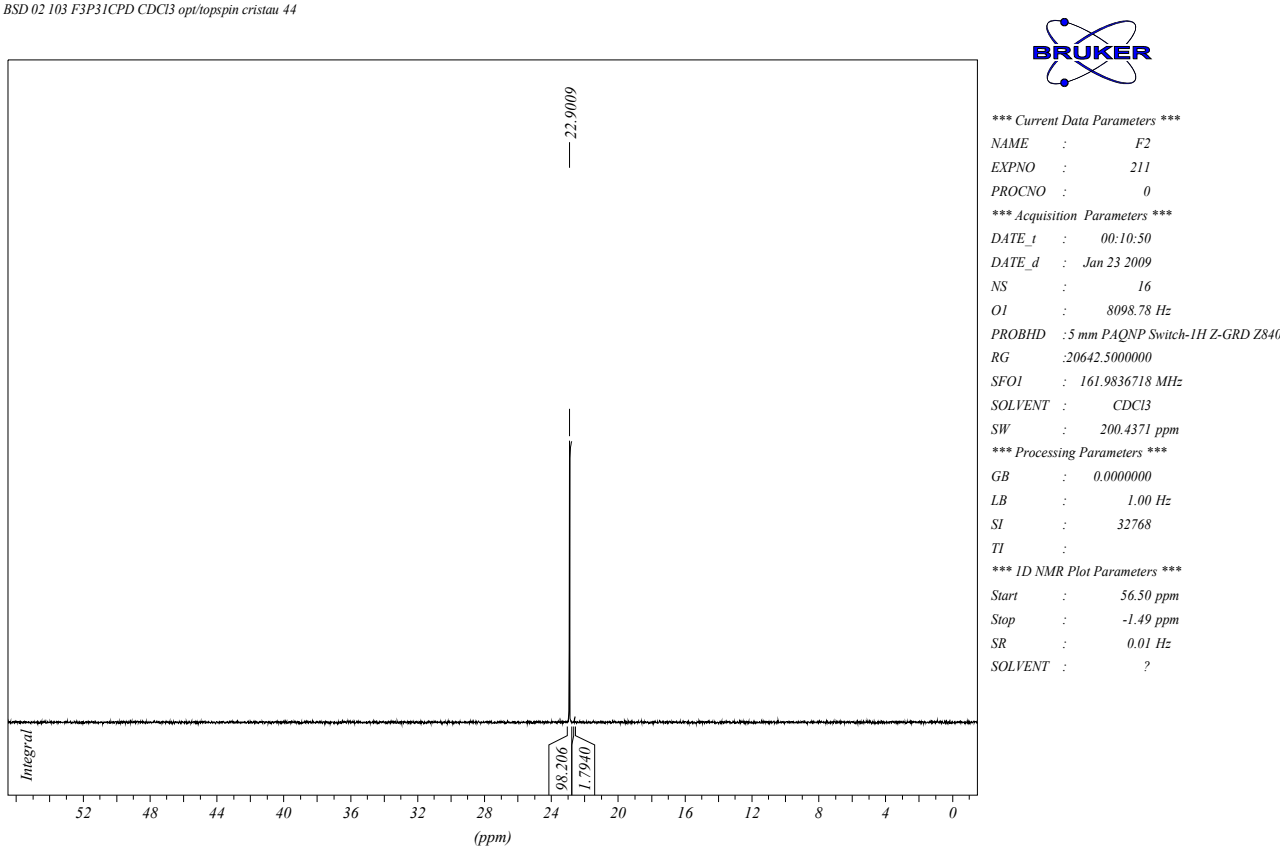
II.5. (±)-Diethyl 2-(2-(benzyloxy)ethoxy)-2-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)ethylphosphonate 10a

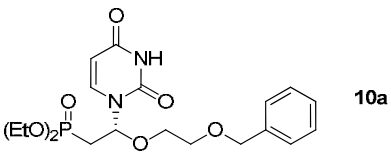


Scheme 3 Reduction and debenzylation steps



$C_{19}H_{27}N_2O_7P$
MW = 426.21 g.mol^{-1}
Colorless oil (398 mg, 85 %)

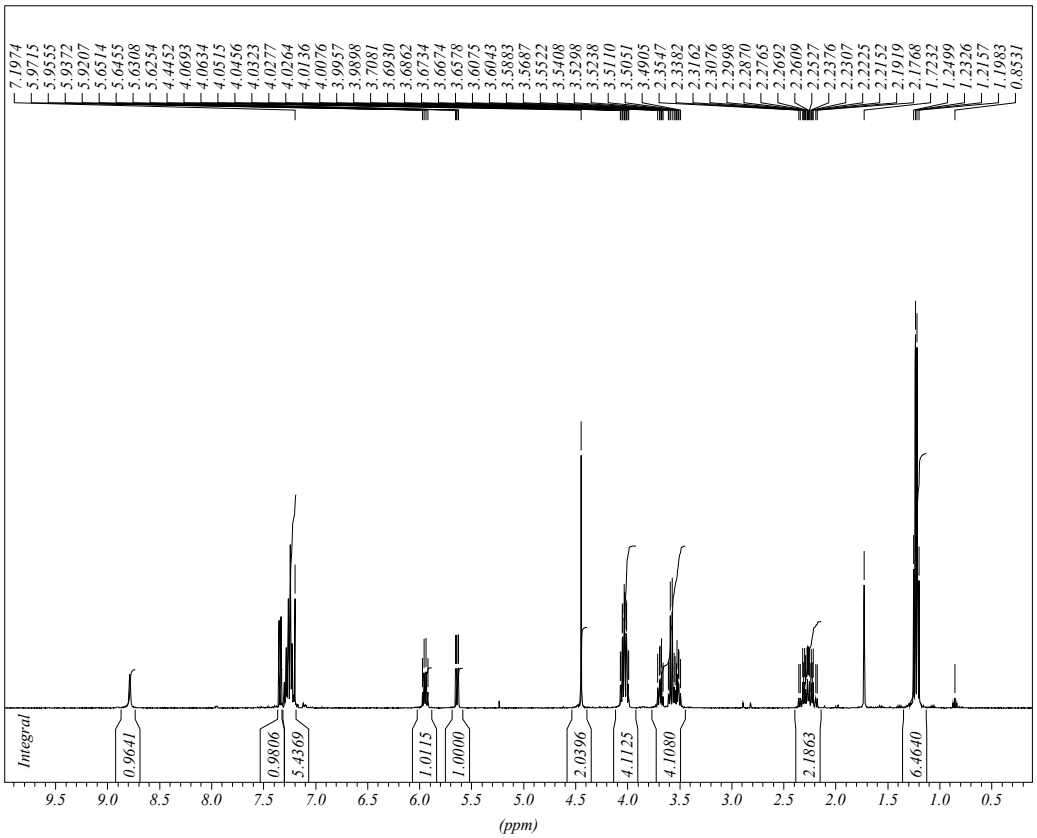




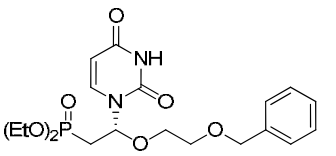
10a

$C_{19}H_{27}N_2O_7P$
MW = 426.21 g.mol^{-1}
Colorless oil (398 mg, 85 %)

BSD 02 103 F2PROTON CDCl3 opt/topspin cristau 39



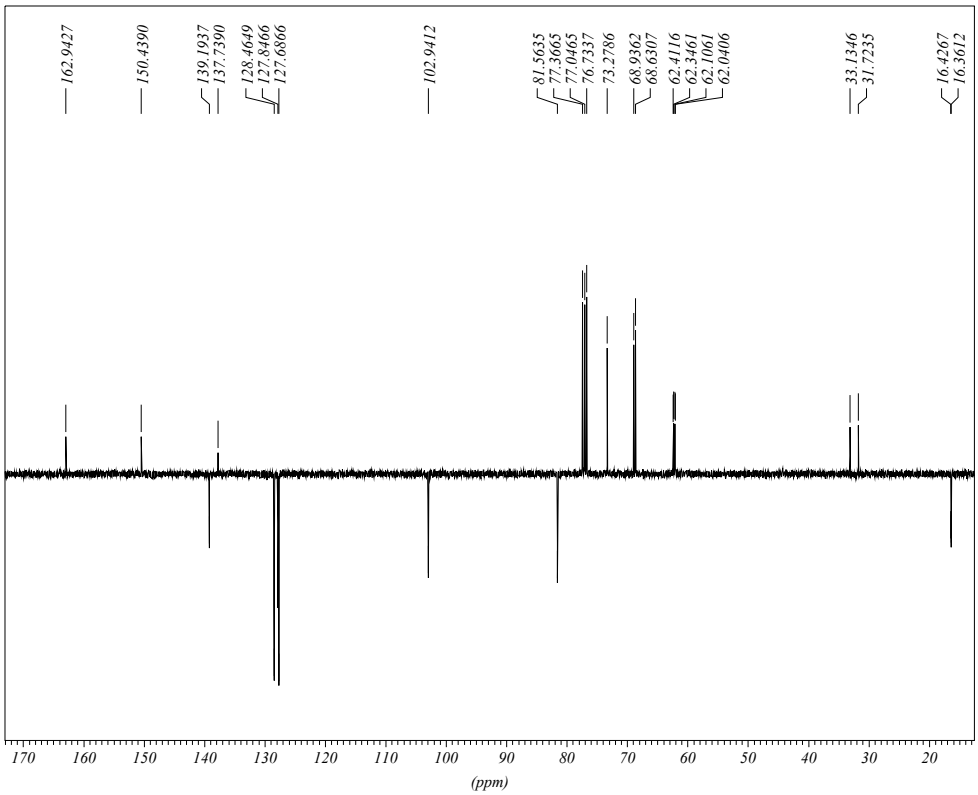
*** Current Data Parameters ***
NAME : sechage1
EXPNO : 212
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 03:35:55
DATE_d : Jan 27 2009
DE : 6.0 usec
DS : 2
NS : 16
NUC1 : 1H
O1 : 2400.78 Hz
O2 : 2470.97 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-GRD Z840
RG : 143.6999969
SFO1 : 400.1324008 MHz
SW : 14.9831 ppm
SW_h : 5995.204 Hz
TD : 65536
*** Processing Parameters ***
GB : 0.0000000
LB : 0.10 Hz
PC : 1.00
SF : 400.1300348 MHz
*** 1D NMR Plot Parameters ***
Start : 9.99 ppm
Stop : 0.11 ppm
SR : 34.82 Hz
ppm_cm : 0.47
Hz_cm : 186.49



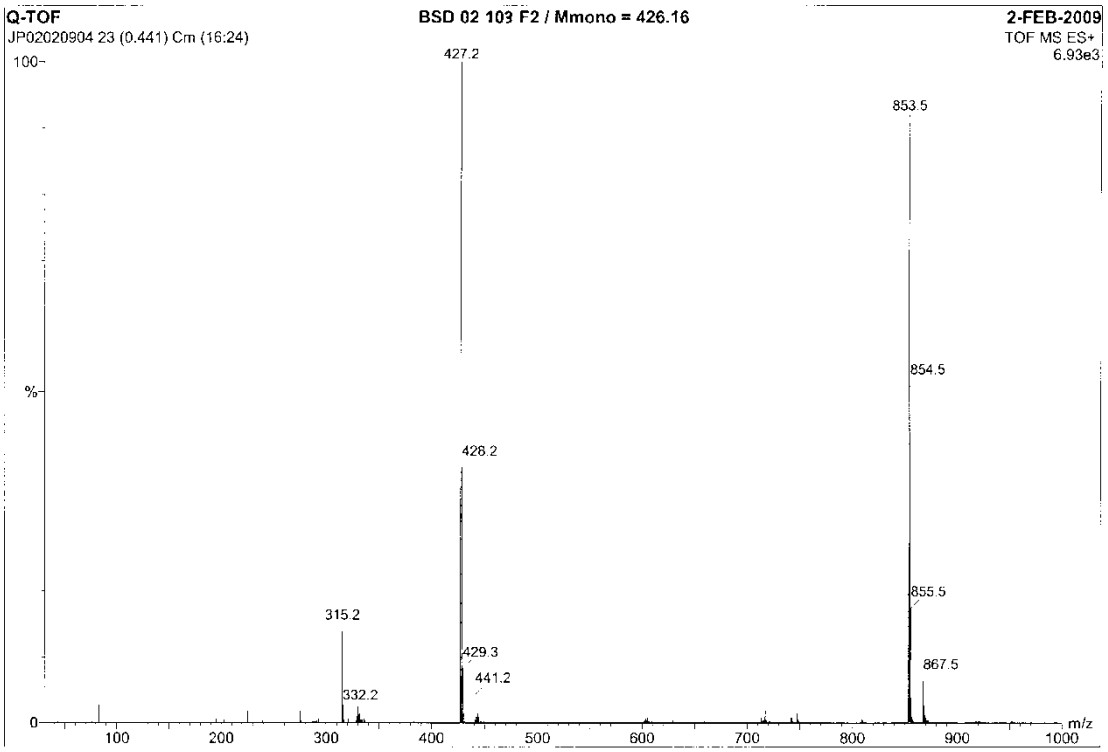
10a

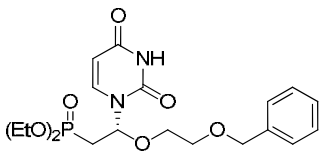
$C_{19}H_{27}N_2O_7P$
MW = 426.21 g.mol^{-1}
Colorless oil (398 mg, 85 %)

BSD 02 103 F2C13APT CDCl3 opt/topspin cristau 39



*** Current Data Parameters ***
NAME : sechage1
EXPNO : 213
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 17:55:34
DATE_d : Jan 27 2009
NS : 1024
O1 : 10060.80 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG :16384.0000000
SFO1 : 100.6228298 MHz
SOLVENT : CDCl3
SW : 238.3238 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 173.06 ppm
Stop : 12.55 ppm
SR : 0.00 Hz
SOLVENT : ?





10a

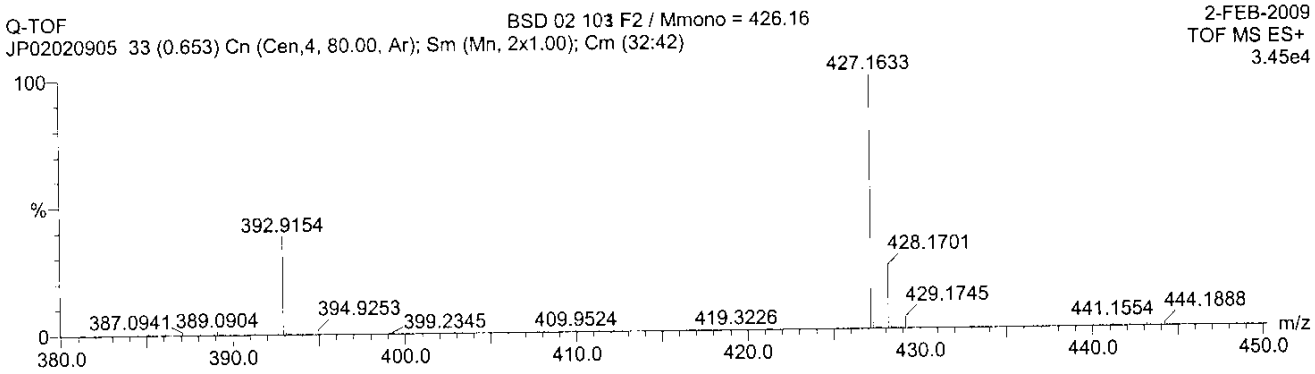
$C_{19}H_{27}N_2O_7P$
MW = 426.21 g.mol^{-1}
Colorless oil (398 mg, 85 %)

Elemental Composition Report

Single Mass Analysis

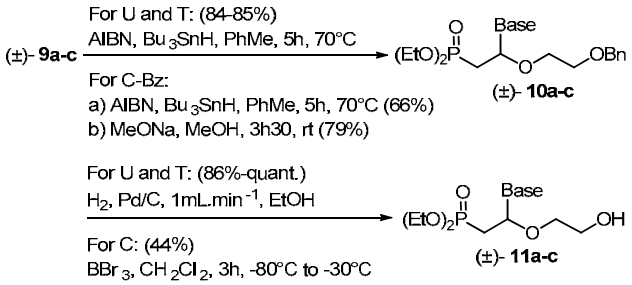
Tolerance = 4.0 mDa / DBE: min = -5.0, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
132 formula(e) evaluated with 4 results within limits (up to 50 closest results for each mass)

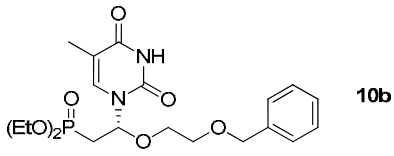


Minimum:				-5.0		
Maximum:		4.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
427.1633	427.1634	-0.1	-0.3	7.5	1	C19 H28 N2 O7 P
	427.1621	1.2	2.9	8.0	2	C17 H26 N5 O6 P
	427.1607	2.6	6.0	3.0	3	C16 H30 N O10 P
	427.1594	3.9	9.1	3.5	4	C14 H28 N4 O9 P

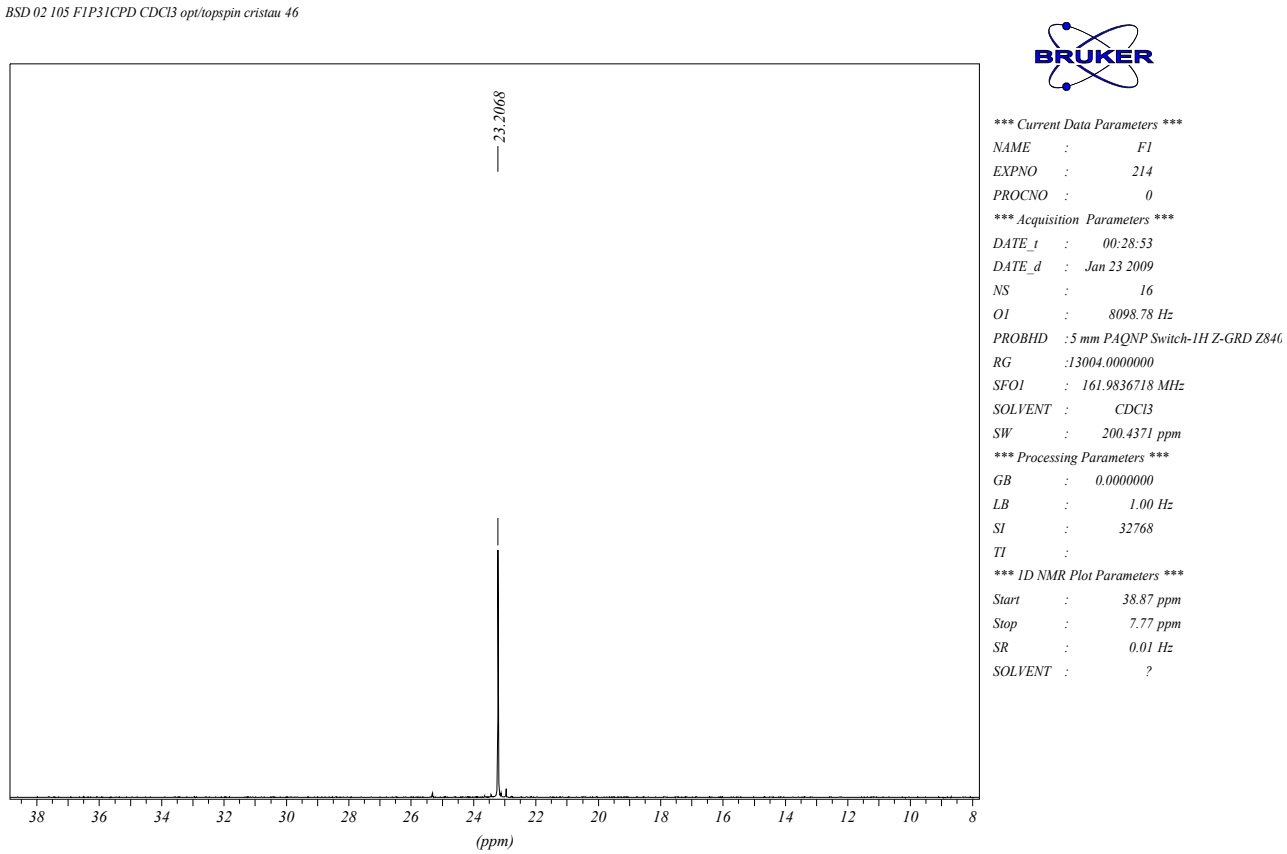
II.6. (±)-Diethyl 2-(2-(benzyloxy)ethoxy)-2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)ethylphosphonate 10b

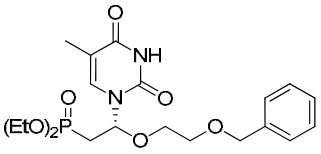


Scheme 3 Reduction and debenzylation steps



$C_{20}H_{29}N_2O_7P$
MW = 440.44 g.mol^{-1}
Colorless (416 mg, 84 %)

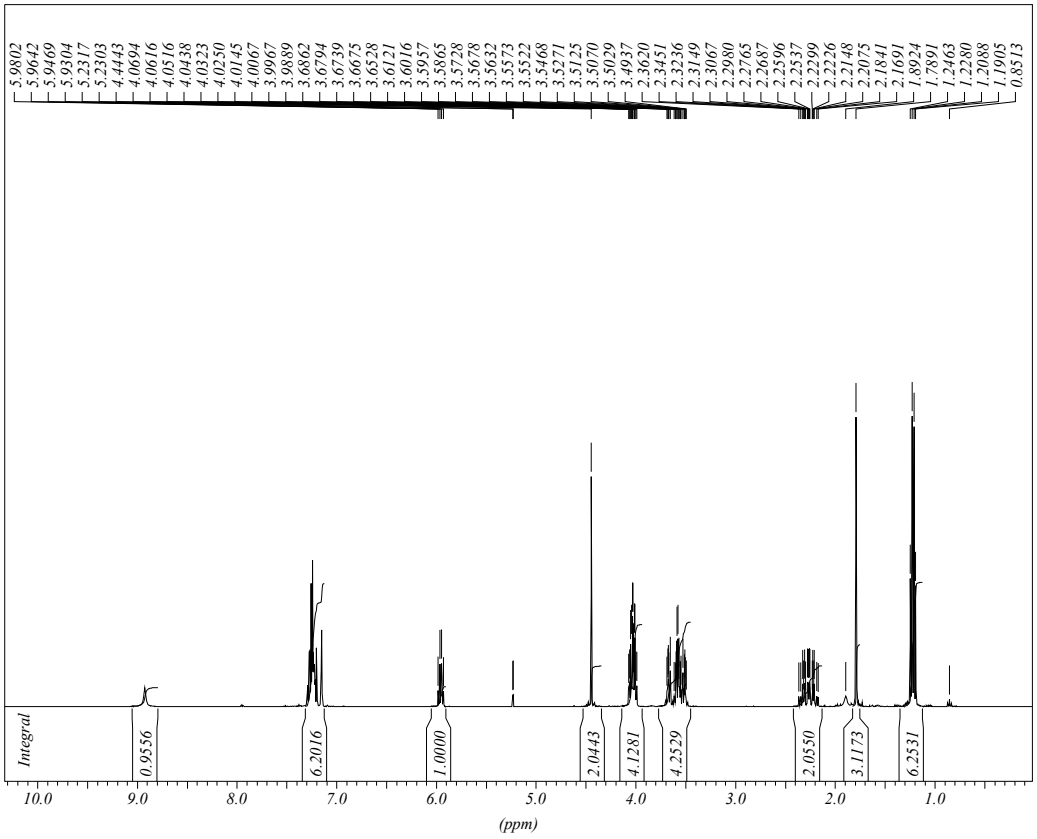




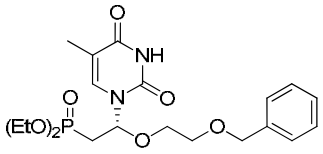
10b

$C_{20}H_{29}N_2O_7P$
MW = 440.44 g.mol^{-1}
Colorless (416 mg, 84 %)

BSD 02 105 F2PROTON CDCl3 opt/topspin cristau 40



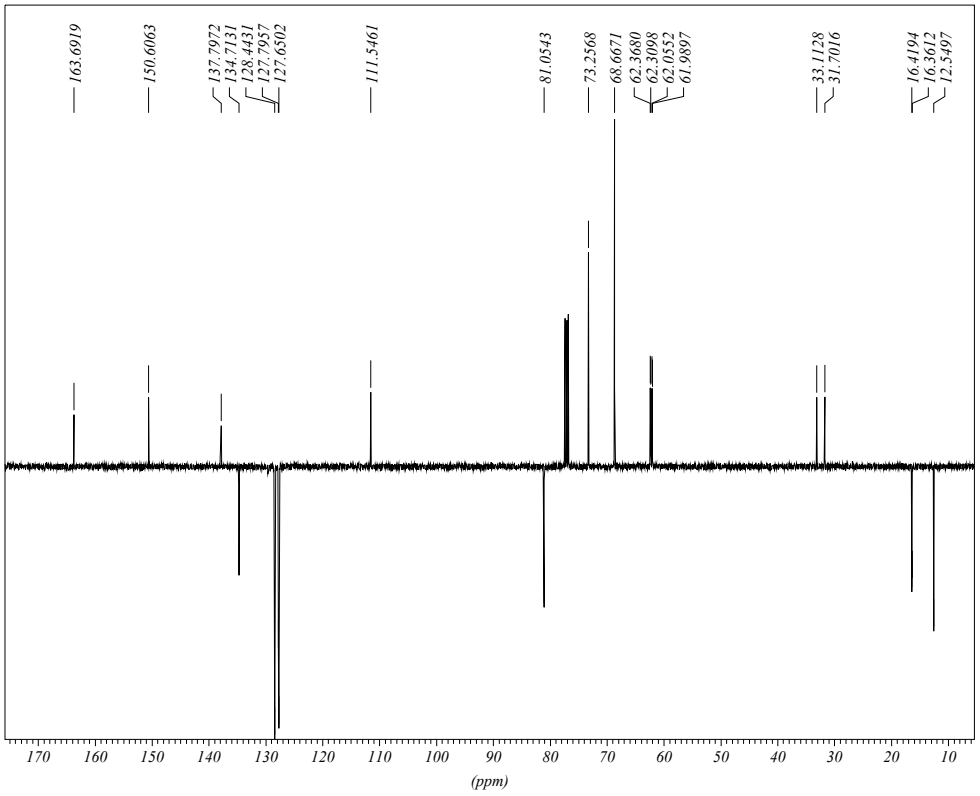
*** Current Data Parameters ***
NAME : sechage1
EXPNO : 214
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 03:43:38
DATE_d : Jan 27 2009
DE : 6.0 usec
DS : 2
NS : 16
NUC1 : 1H
O1 : 2400.78 Hz
O2 : 2470.97 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-GRD Z840
RG : 90.5000000
SFO1 : 400.1324008 MHz
SW : 14.9831 ppm
SW_h : 5995.204 Hz
TD : 65536
*** Processing Parameters ***
GB : 0.0000000
LB : 0.10 Hz
PC : 1.00
SF : 400.1300332 MHz
*** 1D NMR Plot Parameters ***
Start : 10.33 ppm
Stop : 0.02 ppm
SR : 33.16 Hz
ppm_cm : 0.49
Hz_cm : 194.57



10b

$C_{20}H_{29}N_2O_7P$
MW = 440.44 g.mol^{-1}
Colorless (416 mg, 84 %)

BSD 02 105 F2C13APT CDCl3 opt/topspin cristau 40



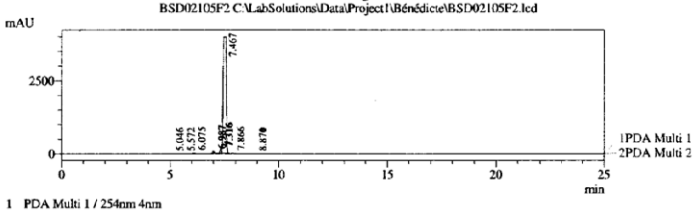
*** Current Data Parameters ***
NAME : sechage1
EXPNO : 215
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 19:00:03
DATE_d : Jan 27 2009
NS : 1024
O1 : 10060.80 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG :23170.5000000
SFO1 : 100.6228298 MHz
SOLVENT : CDCl3
SW : 238.3238 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 175.88 ppm
Stop : 5.42 ppm
SR : 0.00 Hz
SOLVENT : ?

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\Bénédicte\BSD02105F2.lcd

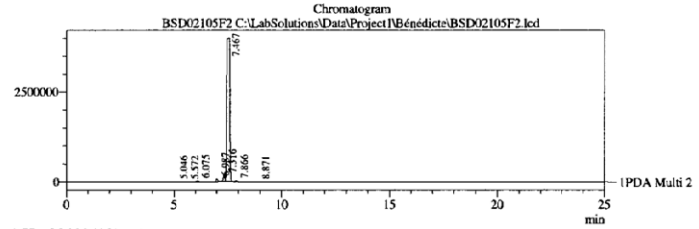
Acquired by	: Admin
Sample Name	: BSD02105F2
Sample ID	: BSD02105F2
Tray#	: 1
Vail #	: 92
Injection Volume	: 10 uL
Data File Name	: BSD02105F2.lcd
Method File Name	: Methode Pierre 2.lcm
Batch File Name	: 26-01-09 grad10-95.lcb
Report File Name	: bene report.lcr
Data Acquired	: 26/01/2009 17:28:43
Data Processed	: 26/01/2009 18:23:57

Chromatogram
BSD02105F2 C:\LabSolutions\Data\Project1\Bénédicte\BSD02105F2.lcd



1 PDA Multi 1 / 254nm 4nm
2 PDA Multi 2 / 264nm 4nm

Chromatogram
BSD02105F2 C:\LabSolutions\Data\Project1\Bénédicte\BSD02105F2.lcd



1 PDA Multi 2 / 264nm 4nm

PeakTable

PDA Ch2 264nm 4nm

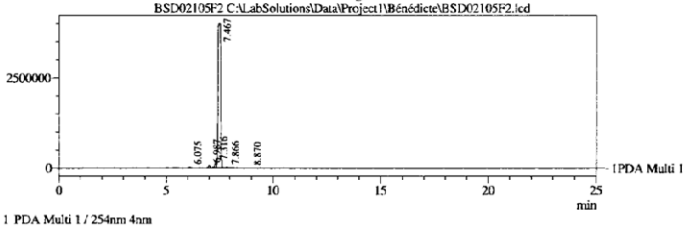
Pic	Temps ret.	Hauteur	Aire	Hauteur %	Aire %
1	5.046	3870	20744	0.090	0.052
2	5.572	2119	14746	0.049	0.037
3	6.075	32734	186728	0.759	0.472
4	6.987	89735	483186	2.080	1.221
5	7.316	169221	863663	3.922	2.183
6	7.467	3983615	37768268	92.319	95.446
7	7.866	31201	217533	0.723	0.550
8	8.871	2548	15259	0.059	0.039
Total		4315042	39570127	100.000	100.000

PeakTable

PDA Ch1 254nm 4nm

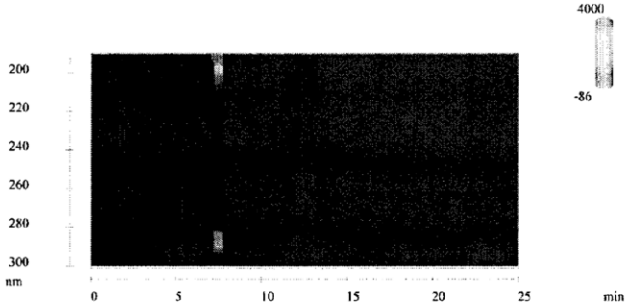
Pic	Temps rét.	Hauteur	Aire	% Hauteur	Area %
1	6.075	20592	99959	0.484	0.267
2	6.987	70409	393384	1.654	1.050
3	7.316	146735	870762	3.447	2.325
4	7.467	3992966	35894164	93.804	95.843
5	7.866	23887	178409	0.561	0.476
6	8.870	2119	14323	0.050	0.038
Total		4256708	37451001	100.000	100.000

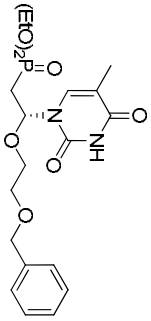
Chromatogram
BSD02105F2 C:\LabSolutions\Data\Project1\Bénédicte\BSD02105F2.lcd



1 PDA Multi 1 / 254nm 4nm

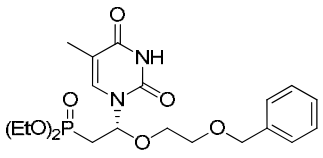
Contour





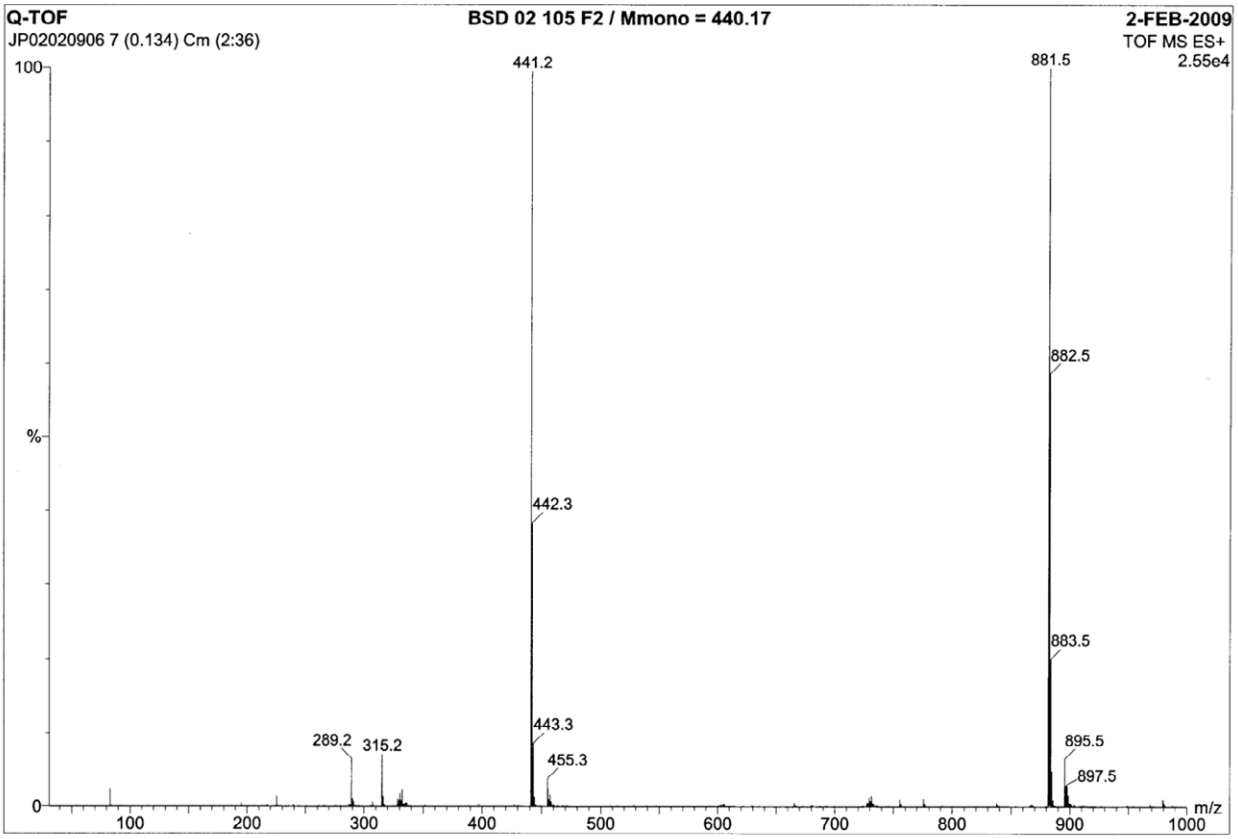
10b

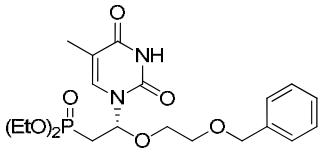
$C_{20}H_{29}N_2O_7P$
MW = 440.44 g.mol^{-1}
Colorless (416 mg, 84 %)



10b

$C_{20}H_{29}N_2O_7P$
MW = 440.44 g.mol^{-1}
Colorless (416 mg, 84 %)





10b

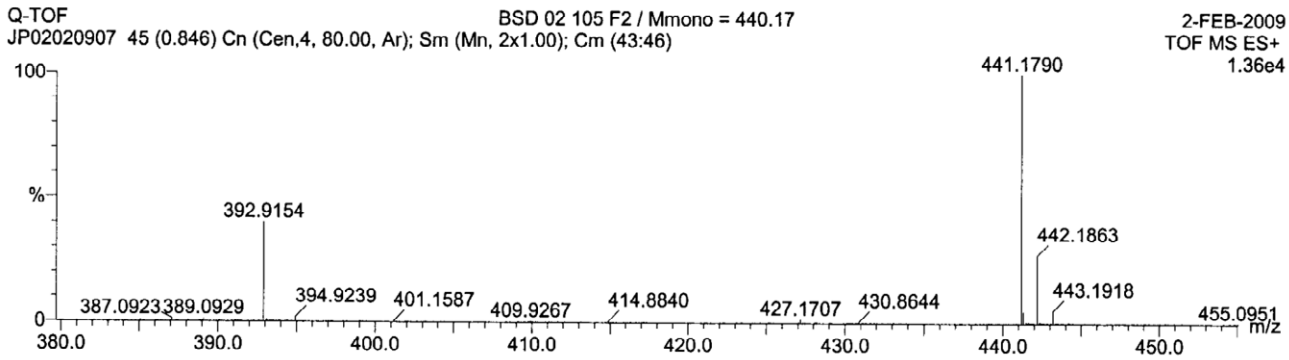
$C_{20}H_{29}N_2O_7P$
MW = 440.44 g.mol^{-1}
Colorless (416 mg, 84 %)

Elemental Composition Report

Single Mass Analysis

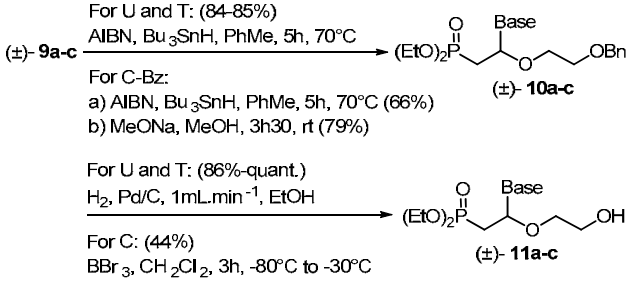
Tolerance = 4.0 mDa / DBE: min = -5.0, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
136 formula(e) evaluated with 4 results within limits (up to 50 closest results for each mass)

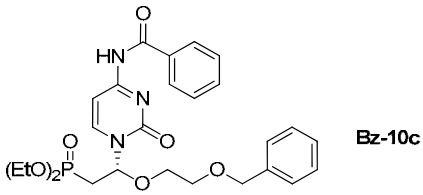


Minimum:				-5.0		
Maximum:		4.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
441.1790	441.1791	-0.1	-0.1	7.5	1	C20 H30 N2 O7 P
	441.1777	1.3	2.9	8.0	2	C18 H28 N5 O6 P
	441.1764	2.6	5.9	3.0	3	C17 H32 N O10 P
	441.1750	4.0	9.0	3.5	4	C15 H30 N4 O9 P

II.7. (±)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-[2-(4-benzoylamino-2-oxo-2H-pyrimidin-1-yl)]ethylphosphonate Bz-10c

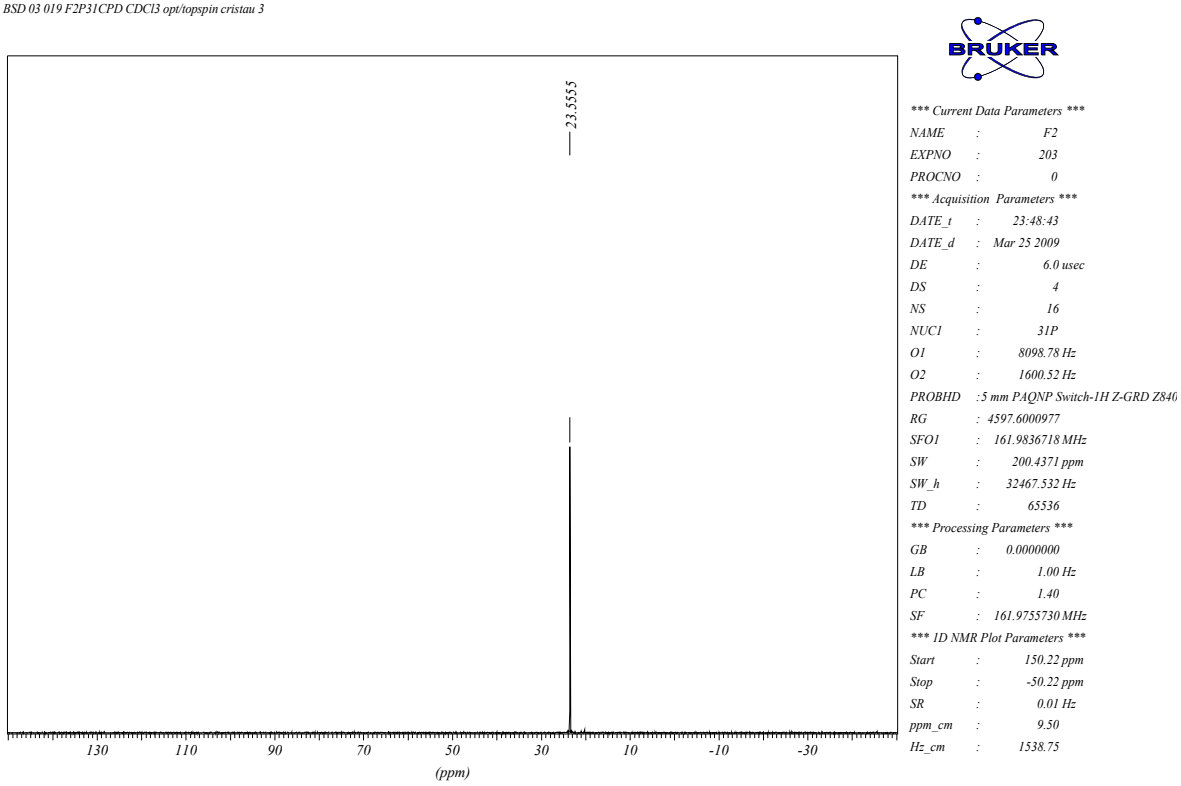


Scheme 3 Reduction and debenzylation steps

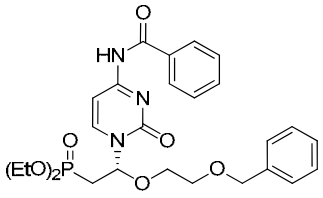


Bz-10c

$C_{26}H_{32}N_3O_7P$
MW = 529.53 g.mol^{-1}
White solid (177 mg, 66 %)

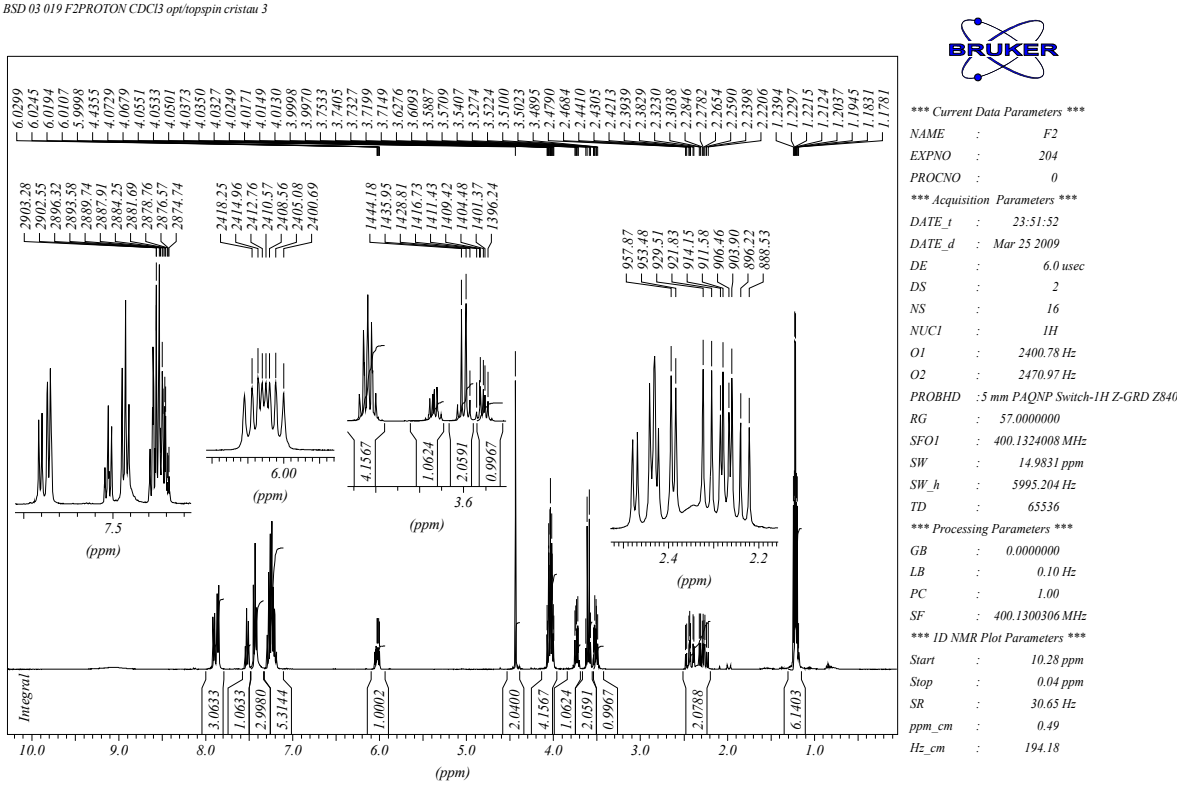


(±)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-[2-(4-benzoylamino-2-oxo-2H-pyrimidin-1-yl)]ethylphosphonate Bz-10c

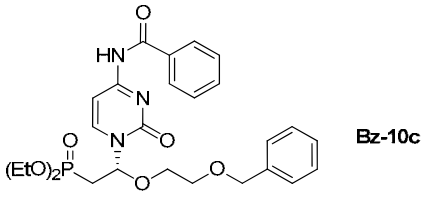


Bz-10c

$C_{26}H_{32}N_3O_7P$
MW = 529.53 g.mol^{-1}
White solid (177 mg, 66 %)

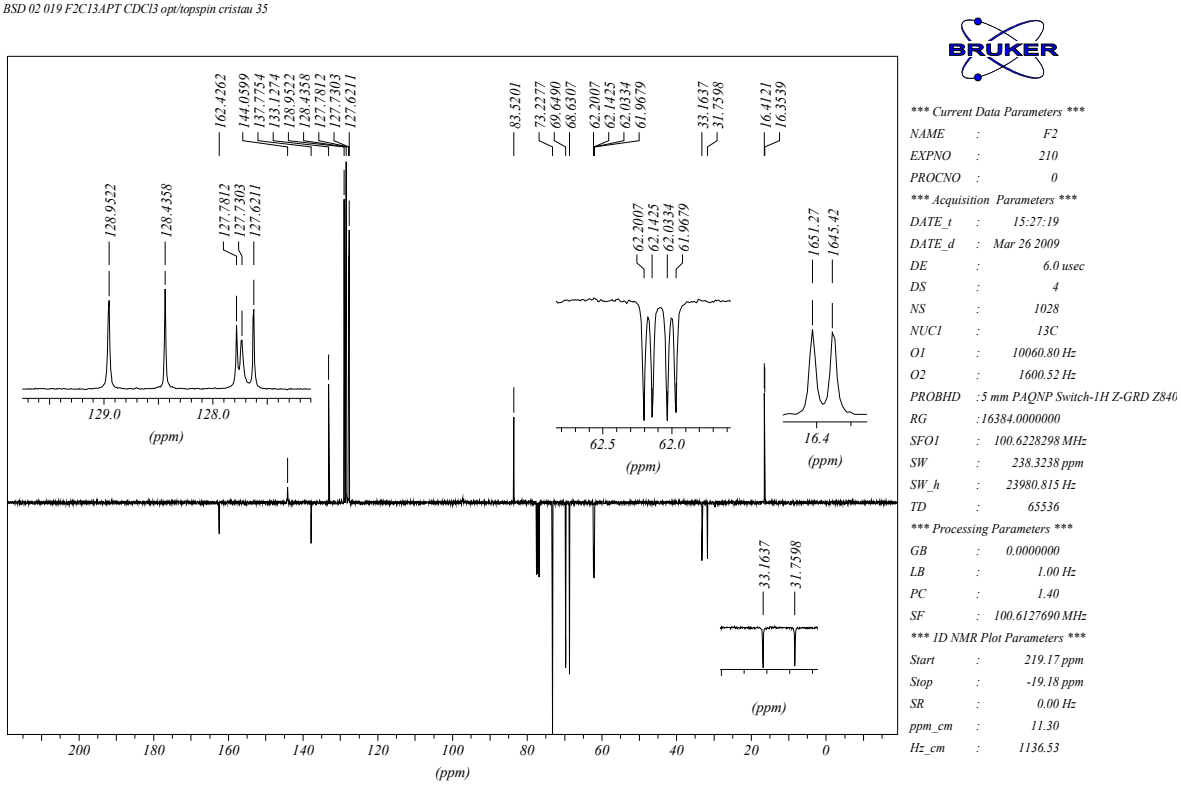


(±)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-[2-(4-benzoylamino-2-oxo-2H-pyrimidin-1-yl)]ethylphosphonate Bz-10c



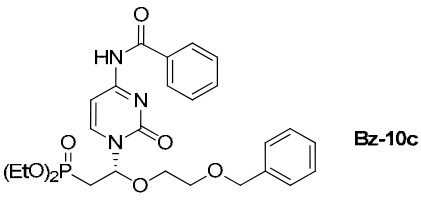
Bz-10c

$C_{26}H_{32}N_3O_7P$
MW = 529.53 g.mol^{-1}
White solid (177 mg, 66 %)



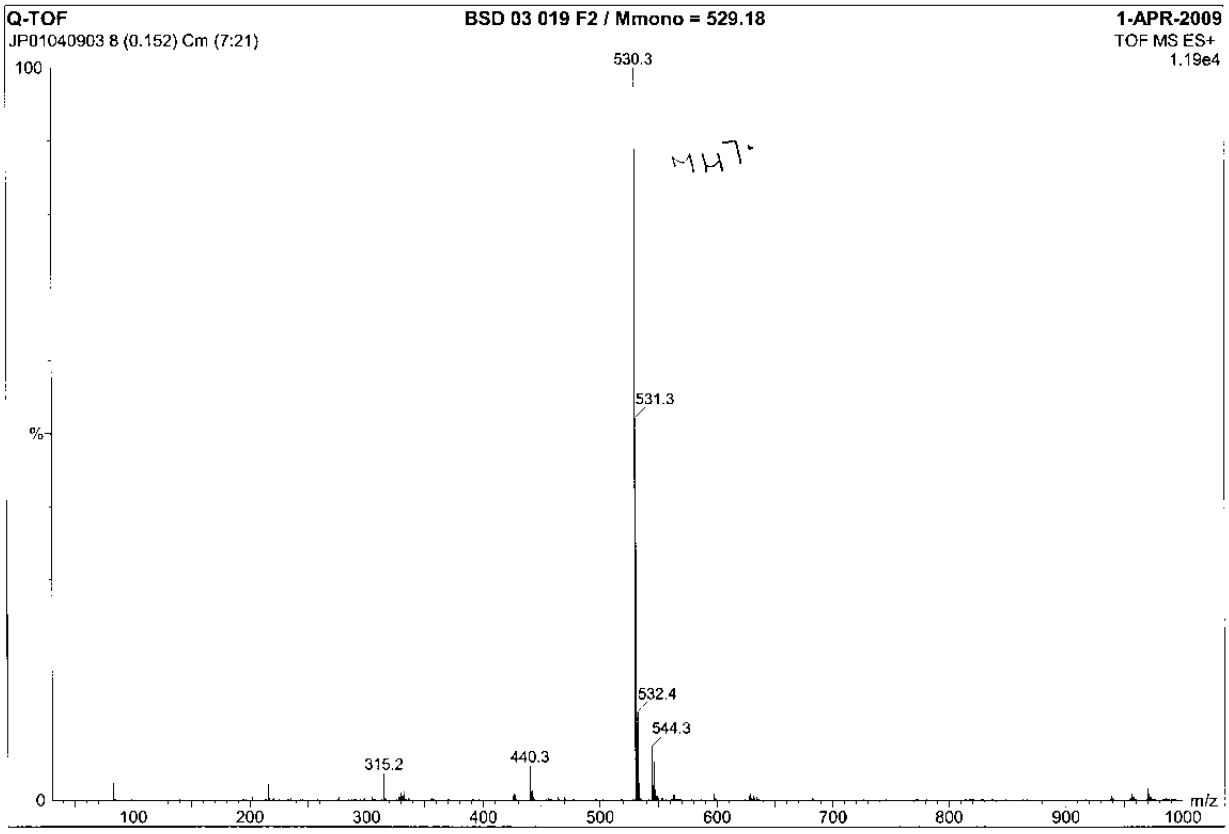
*** Current Data Parameters ***
NAME : F2
EXPNO : 210
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 15:27:19
DATE_d : Mar 26 2009
DE : 6.0 usec
DS : 4
NS : 1028
NUC1 : 13C
O1 : 10060.80 Hz
O2 : 1600.52 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-GRD Z840
RG : 16384.0000000
SFO1 : 100.6228298 MHz
SW : 238.3238 ppm
SW_h : 23980.815 Hz
TD : 65536
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
PC : 1.40
SF : 100.6127690 MHz
*** 1D NMR Plot Parameters ***
Start : 219.17 ppm
Stop : -19.18 ppm
SR : 0.00 Hz
ppm_cm : 11.30
Hz_cm : 1136.53

(±)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-[2-(4-benzoylamino-2-oxo-2H-pyrimidin-1-yl)]ethylphosphonate <u>Bz-10c</u>

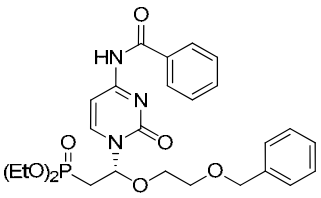


Bz-10c

$C_{26}H_{32}N_3O_7P$
MW = 529.53 g.mol^{-1}
White solid (177 mg, 66 %)



(±)-Diethyl 2-[2-(benzyloxy)ethoxy]-2-[2-(4-benzoylamino-2-oxo-2H-pyrimidin-1-yl)]ethylphosphonate Bz-10c



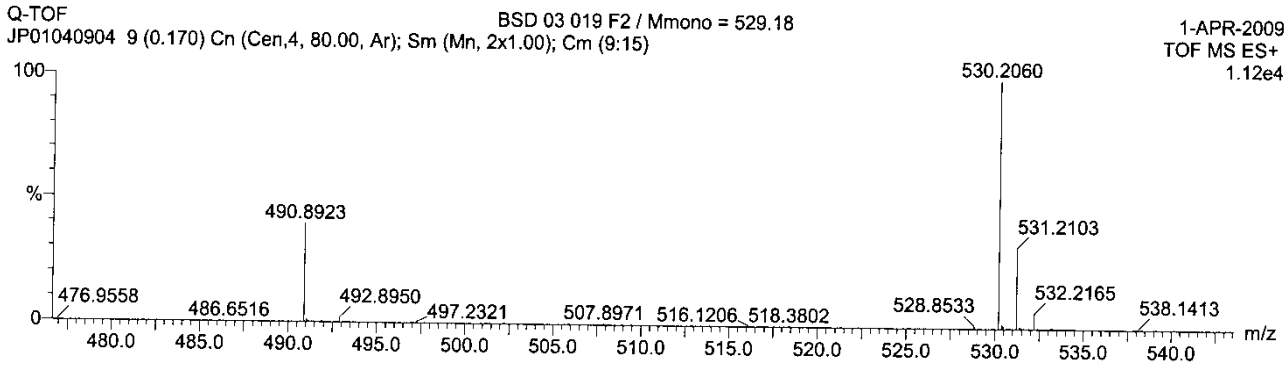
Bz-10c

$C_{26}H_{32}N_3O_7P$
MW = 529.53 g.mol^{-1}
White solid (177 mg, 66 %)

Elemental Composition Report **Page 1**

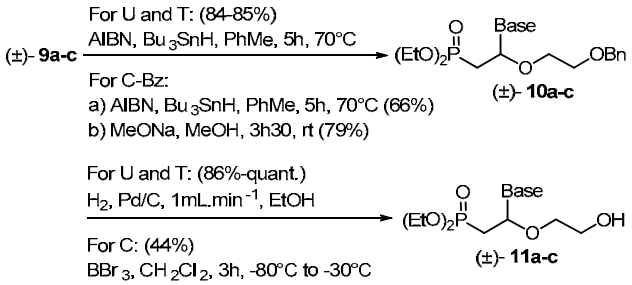
Single Mass Analysis (displaying only valid results)
Tolerance = 3.0 mDa / DBE: min = -5.0, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
126 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

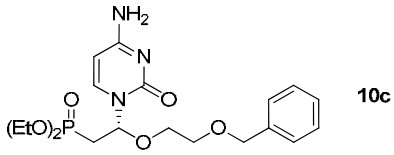


Minimum:				-5.0		
Maximum:		3.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
530.2060	530.2056	0.4	0.7	12.5	1	C26 H33 N3 O7 P

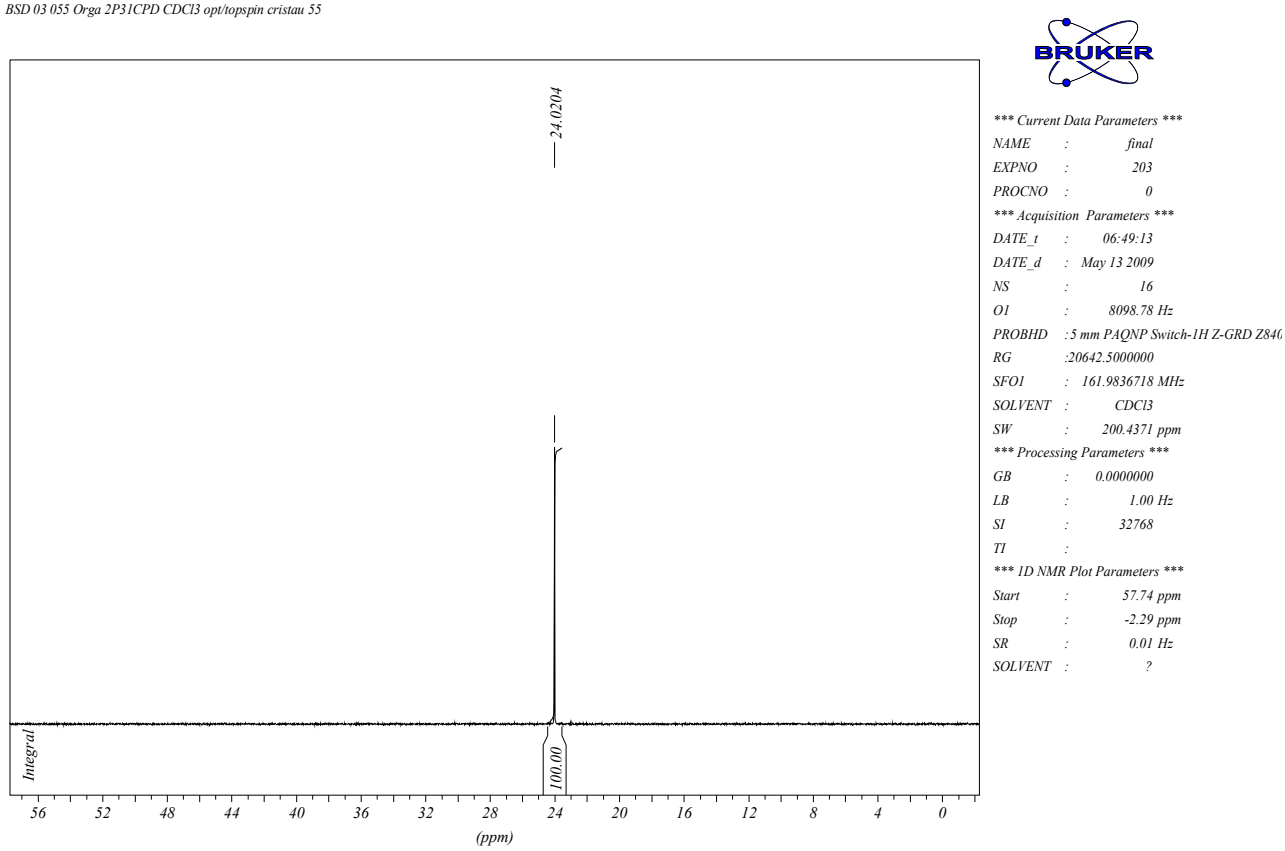
II.8. *(±)*-Diethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-[2-(benzyloxy)ethoxy]ethylphosphonate 10c



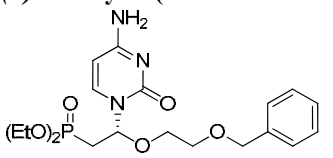
Scheme 3 Reduction and debenzylation steps



$C_{19}H_{28}N_3O_6P$
MW = 425.43 g.mol^{-1}
Colorless oil (240 mg, 79 %)



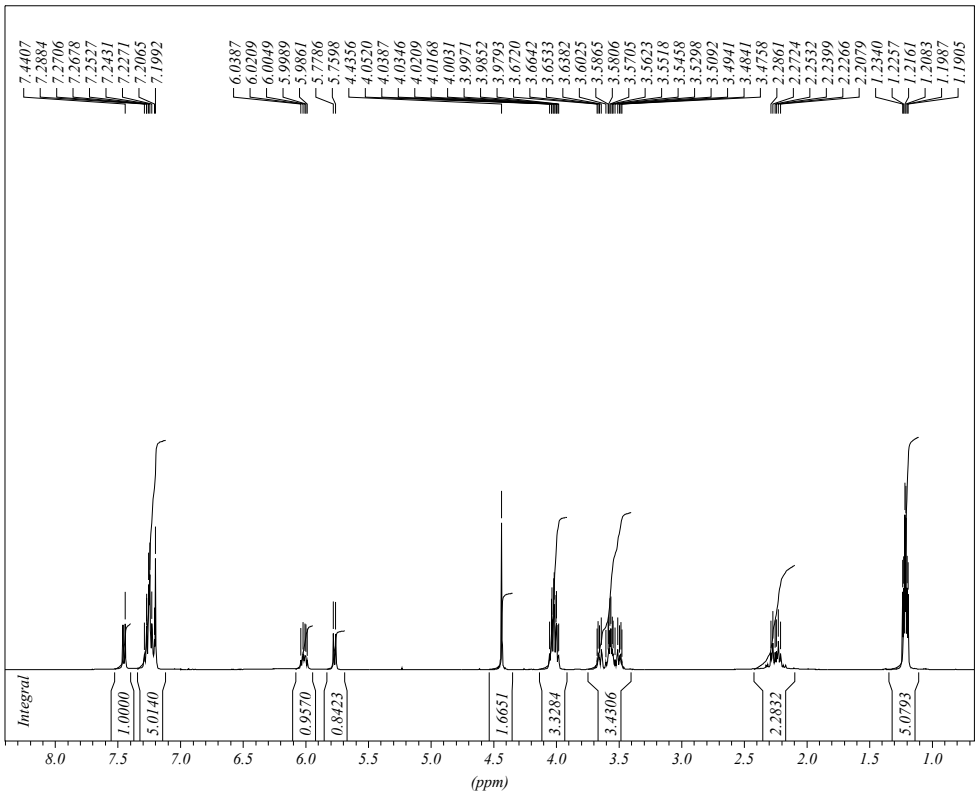
(±)-Diethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-[2-(benzyloxy)ethoxy]ethylphosphonate 10c



10c

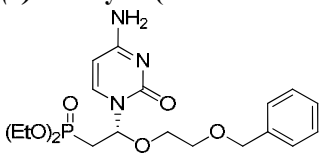
$C_{19}H_{28}N_3O_6P$
MW = 425.43 g.mol^{-1}
Colorless oil (240 mg, 79 %)

BSD 03 055 Orga 2PROTON CDCl3 opt/topspin cristau 55



*** Current Data Parameters ***
NAME : final
EXPNO : 204
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 06:52:33
DATE_d : May 13 2009
NS : 16
O1 : 2400.78 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG : 161.3000031
SFO1 : 400.1324008 MHz
SOLVENT : CDCl3
SW : 14.9831 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 8.40 ppm
Stop : 0.66 ppm
SR : 34.45 Hz
SOLVENT : ?

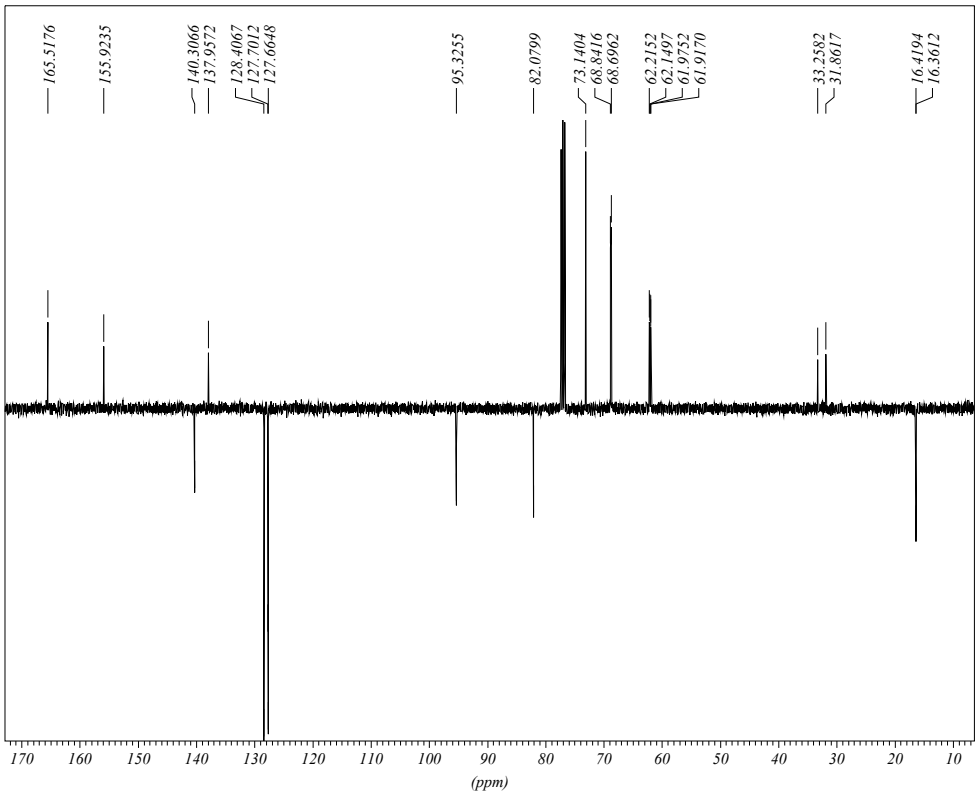
(±)-Diethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-[2-(benzyloxy)ethoxy]ethylphosphonate 10c



10c

$C_{19}H_{28}N_3O_6P$
MW = 425.43 g.mol^{-1}
Colorless oil (240 mg, 79 %)

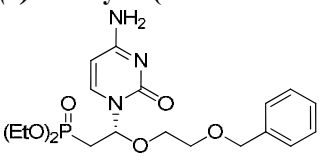
BSD 03 055 Orga 2C13APT CDCl3 opt/topspin cristau 55



BRUKER

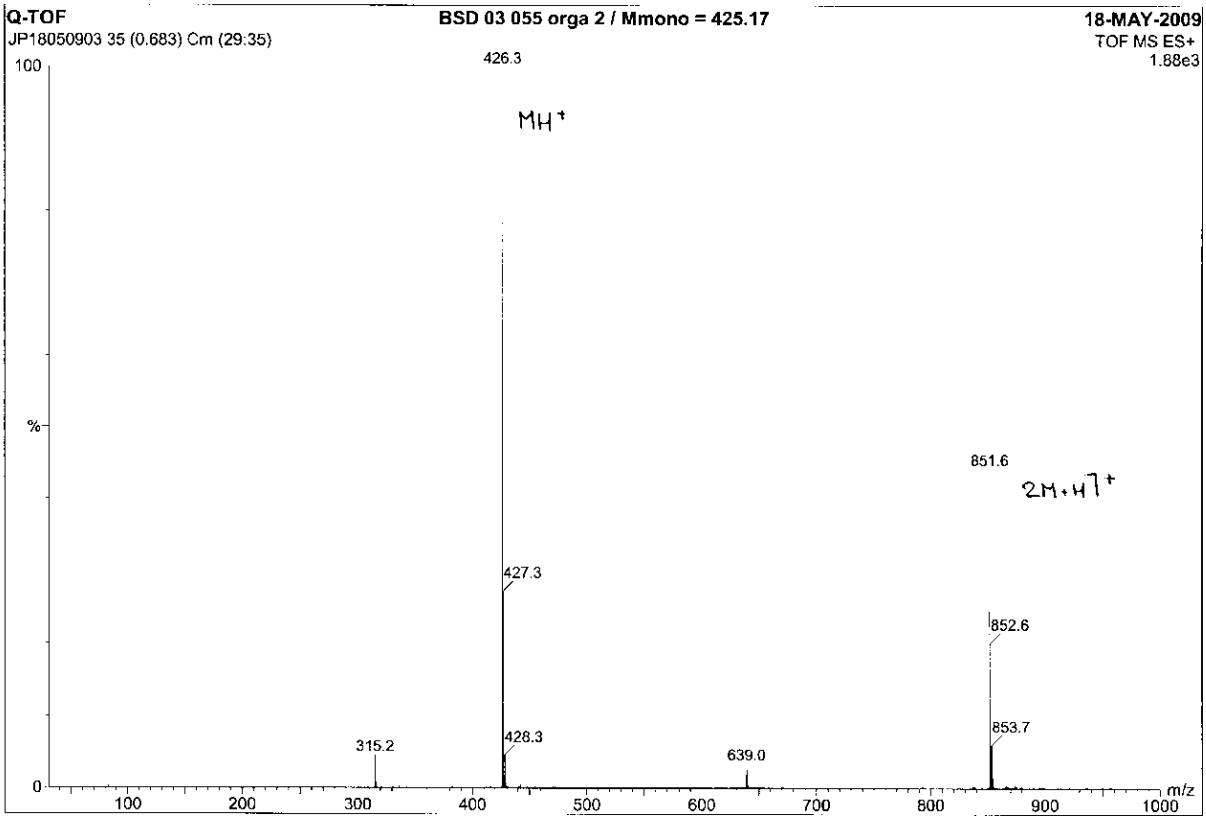
*** Current Data Parameters ***
NAME : final
EXPNO : 205
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 13:00:17
DATE_d : May 13 2009
NS : 1024
O1 : 10060.80 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG :16384.0000000
SFO1 : 100.6228298 MHz
SOLVENT : CDCl3
SW : 238.3238 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 172.92 ppm
Stop : 6.37 ppm
SR : 0.00 Hz
SOLVENT : ?

***(±)*-Diethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-[2-(benzyloxy)ethoxy]ethylphosphonate <u>10c</u>**

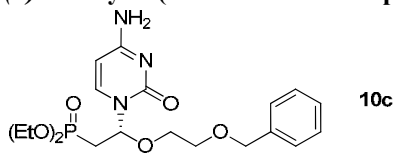


10c

$C_{19}H_{28}N_3O_6P$
MW = 425.43 g.mol^{-1}
Colorless oil (240 mg, 79 %)



(±)-Diethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-[2-(benzyloxy)ethoxy]ethylphosphonate 10c



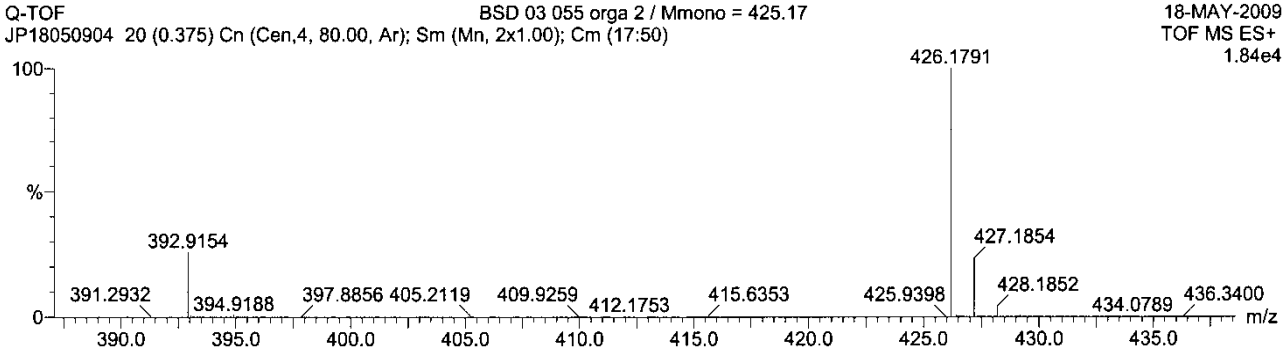
10c

$C_{19}H_{28}N_3O_6P$
MW = 425.43 g.mol^{-1}
Colorless oil (240 mg, 79 %)

Elemental Composition Report **Page 1**

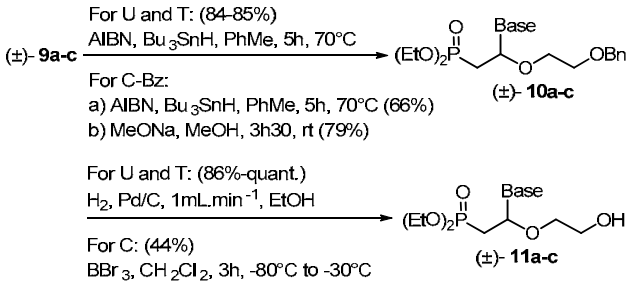
Single Mass Analysis (displaying only valid results)
Tolerance = 3.0 mDa / DBE: min = -5.0, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
133 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)

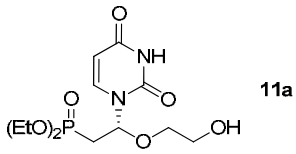


Minimum:				-5.0		
Maximum:		3.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
426.1791	426.1794	-0.3	-0.7	7.5	1	C19 H29 N3 O6 P
	426.1767	2.4	5.6	3.0	2	C16 H31 N2 O9 P

II.9. *(±)*-Diethyl 2-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11a



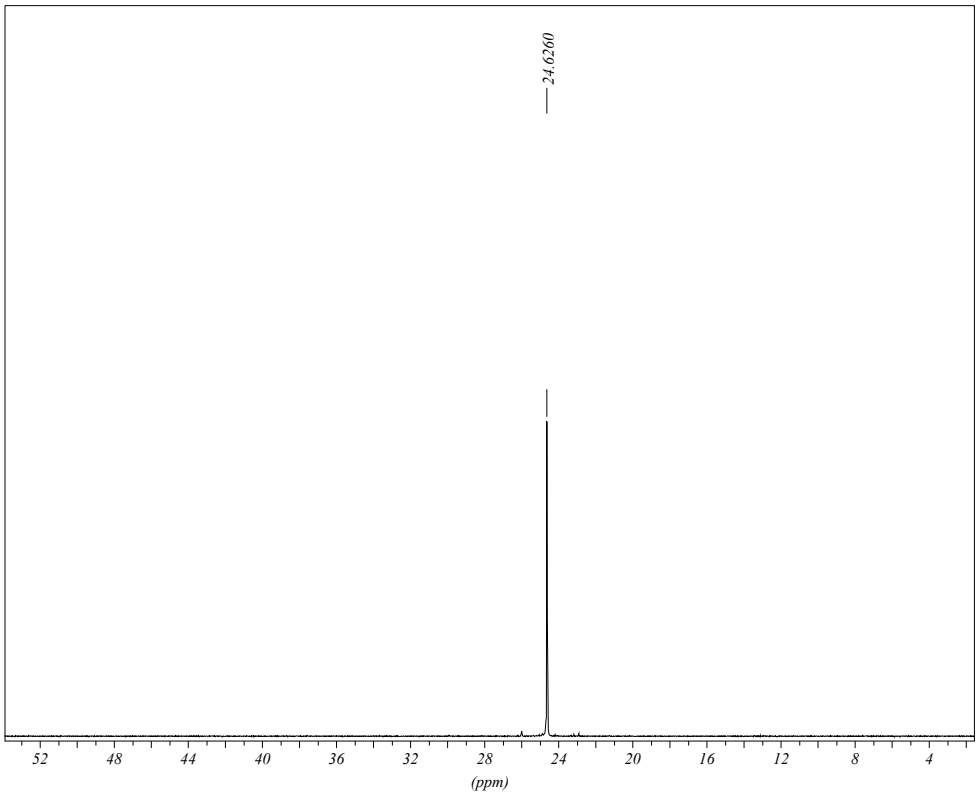
Scheme 3 Reduction and debenzylation steps



11a

$C_{12}H_{21}N_2O_7P$
MW = 336.28 g.mol^{-1}
Colorless (43 mg, quantitative yield)

BSD 02 115-1P31CPD CDCl3 opt/topspin cristau 34



BRUKER

*** Current Data Parameters ***
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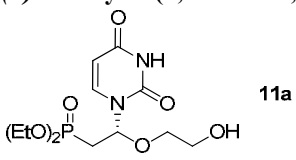
EXPNO : 201
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 07:33:45
DATE_d : Feb 02 2009
NS : 16
O1 : 8098.78 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-GRD Z840
RG : 10321.2998047
SFO1 : 161.9836718 MHz
SOLVENT : CDCl3
SW : 200.4371 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 53.90 ppm
Stop : 1.56 ppm
SR : 0.01 Hz
SOLVENT : ?

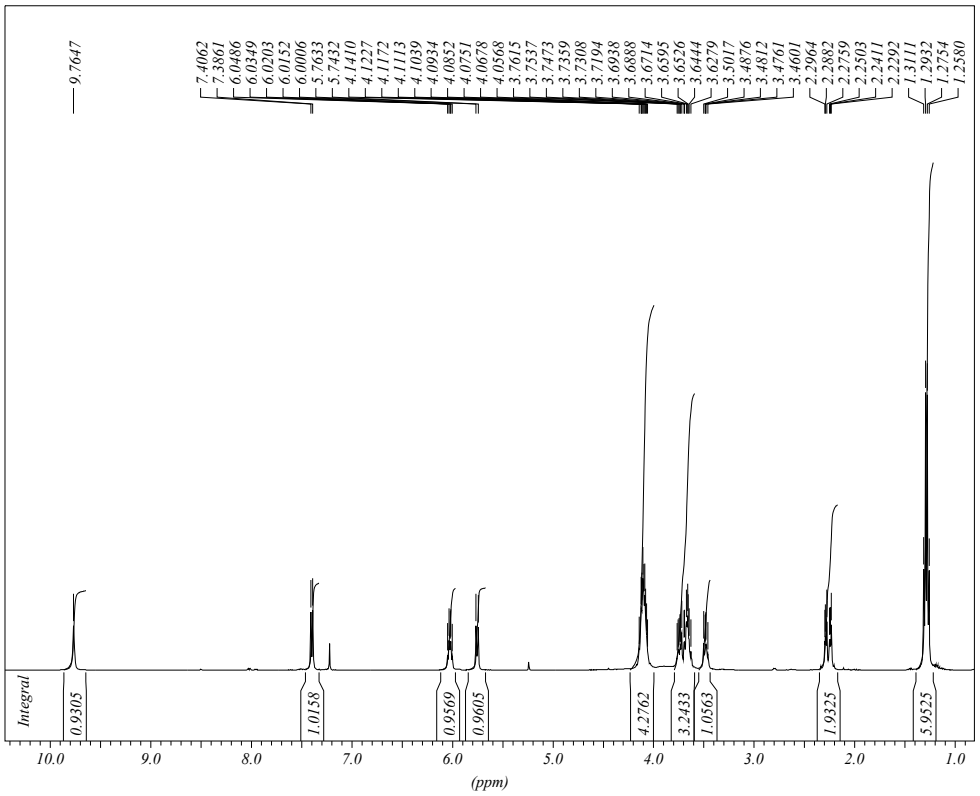
(±)-Diethyl 2-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11a



11a

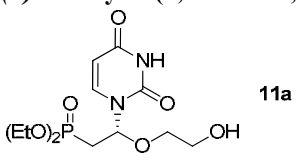
$C_{12}H_{21}N_2O_7P$
MW = 336.28 g.mol^{-1}
Colorless (43 mg, quantitative yield)

BSD 02 115-2PROTON CDCl3 opt/topspin cristau 28



*** Current Data Parameters ***
NAME : sech2
EXPNO : 201
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 03:37:52
DATE_d : Feb 13 2009
NS : 16
O1 : 2400.78 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG : 80.5999985
SFO1 : 400.1324008 MHz
SOLVENT : CDCl3
SW : 14.9831 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 10.45 ppm
Stop : 0.81 ppm
SR : 26.28 Hz
SOLVENT : ?

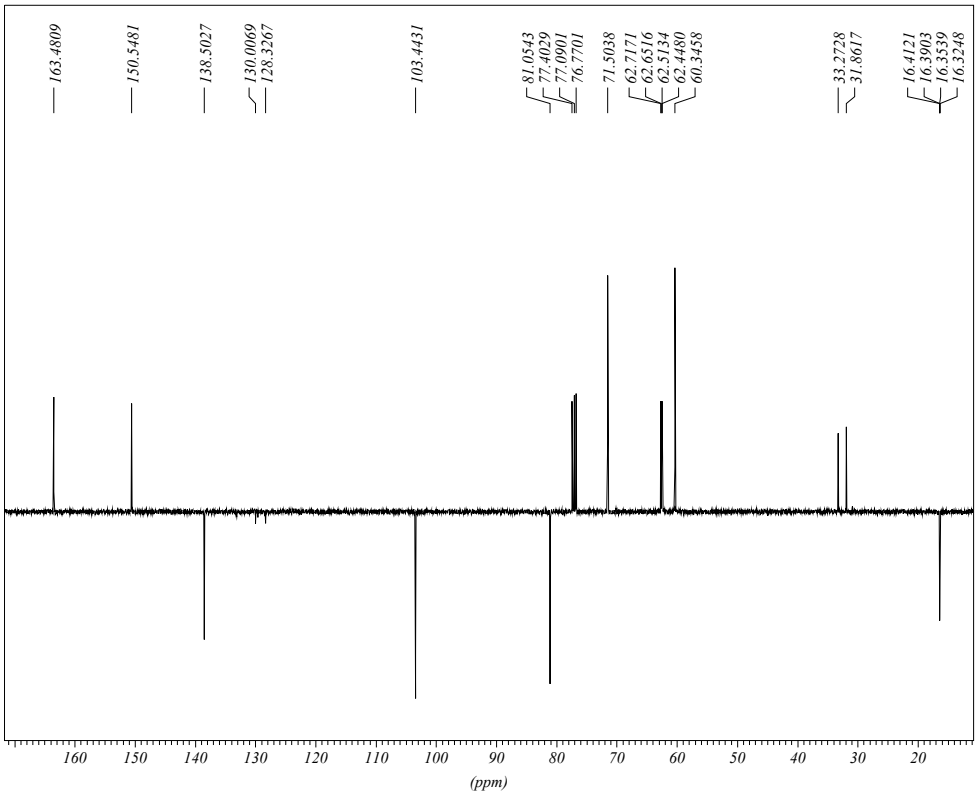
(±)-Diethyl 2-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11a



11a

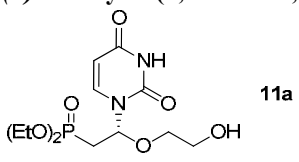
$C_{12}H_{21}N_2O_7P$
MW = 336.28 g.mol^{-1}
Colorless (43 mg, quantitative yield)

BSD 02 115C13APT CDCl3 opt/topspin cristau 14



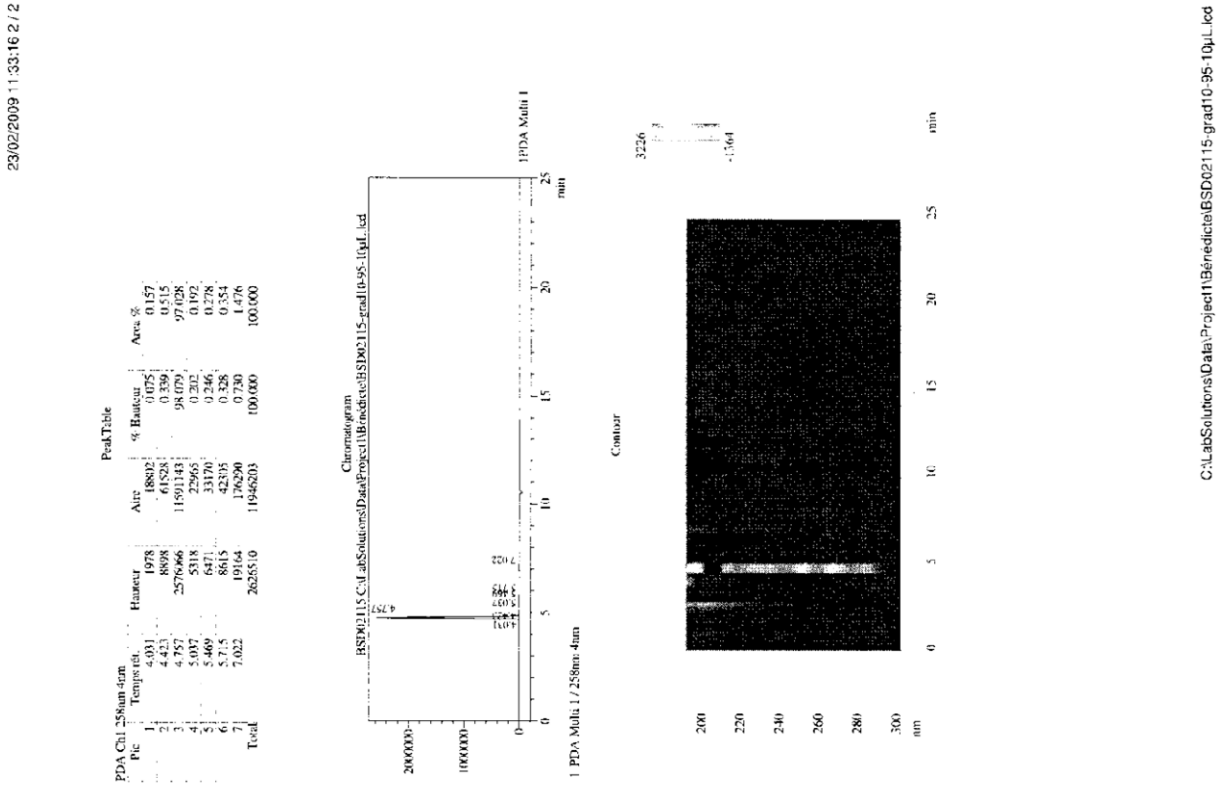
*** Current Data Parameters ***
NAME : 13C
EXPNO : 230
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 13:57:25
DATE_d : Feb 19 2009
NS : 1024
O1 : 10060.80 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG :16384.0000000
SFO1 : 100.6228298 MHz
SOLVENT : CDCl3
SW : 238.3238 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 171.71 ppm
Stop : 10.80 ppm
SR : 0.00 Hz
SOLVENT : ?

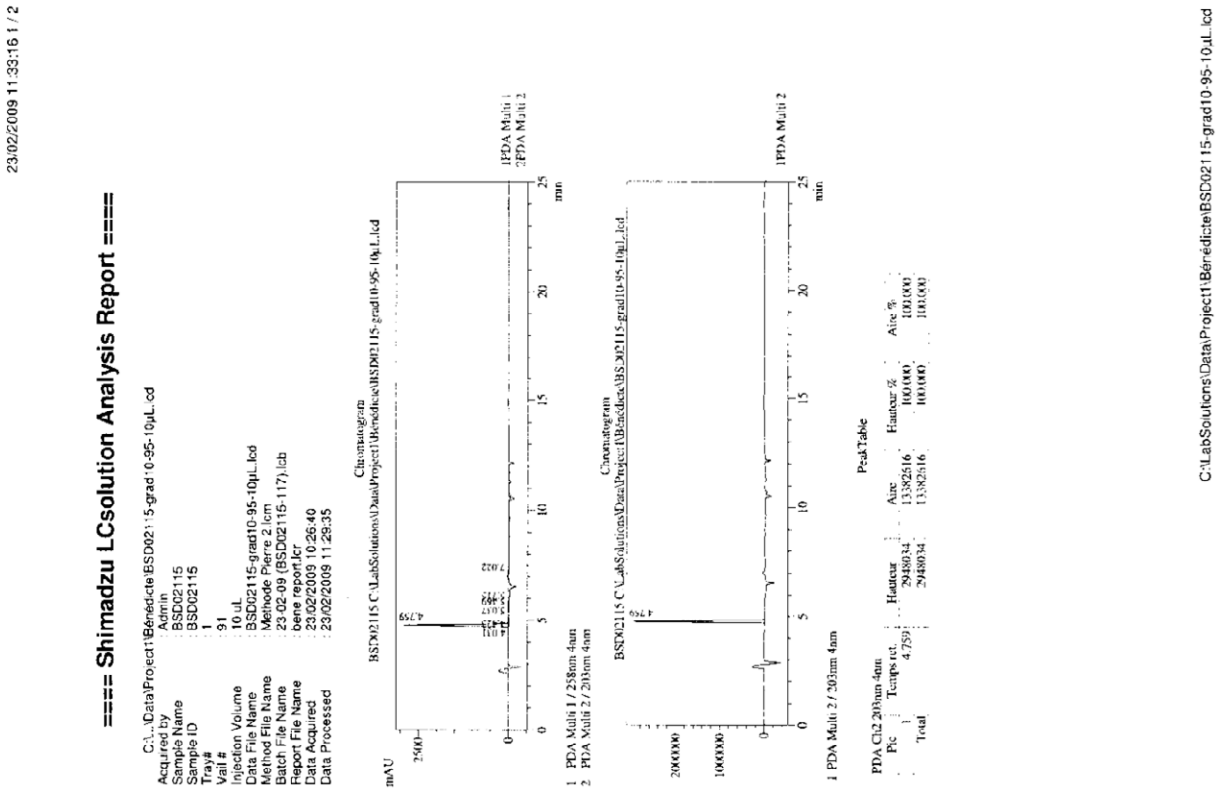
(±)-Diethyl 2-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11a



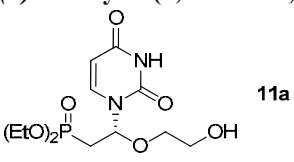
11a

$C_{12}H_{21}N_2O_7P$
MW = 336.28 g.mol^{-1}
Colorless (43 mg, quantitative yield)



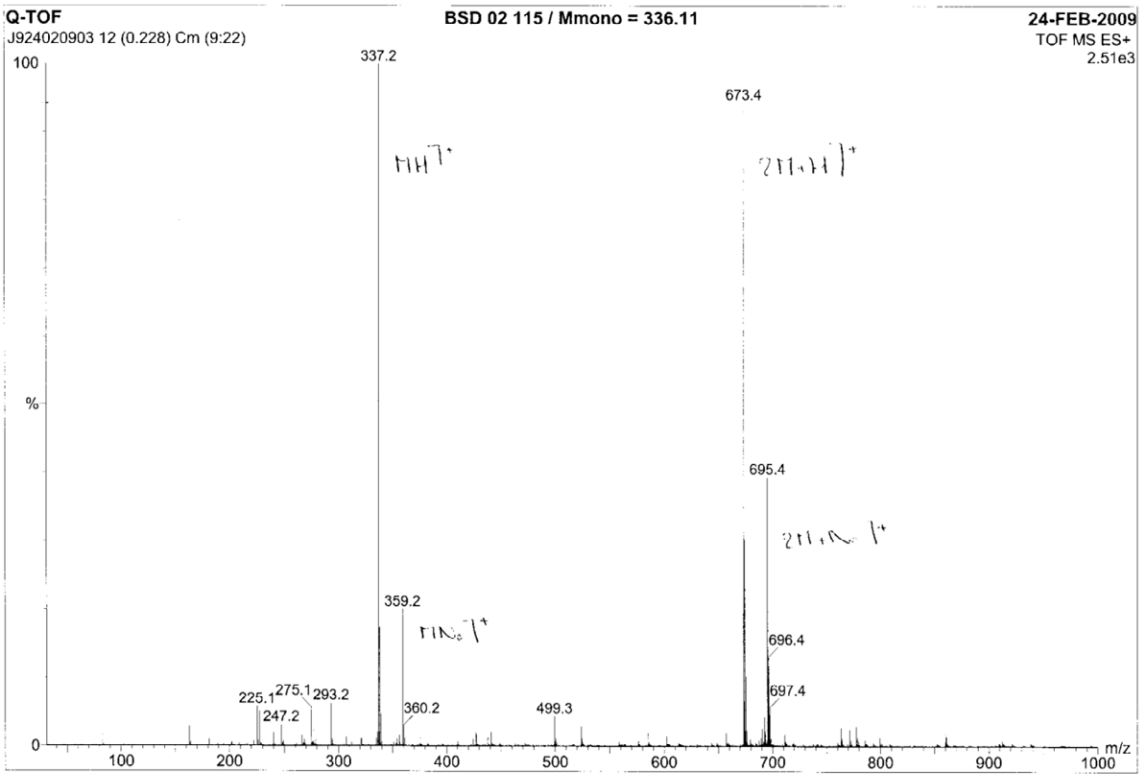


(±)-Diethyl 2-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11a

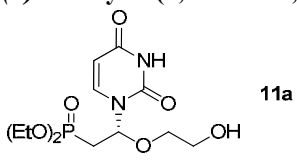


11a

$C_{12}H_{21}N_2O_7P$
MW = 336.28 g.mol^{-1}
Colorless (43 mg, quantitative yield)



(±)-Diethyl 2-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11a



11a

$C_{12}H_{21}N_2O_7P$
MW = 336.28 g.mol^{-1}
Colorless (43 mg, quantitative yield)

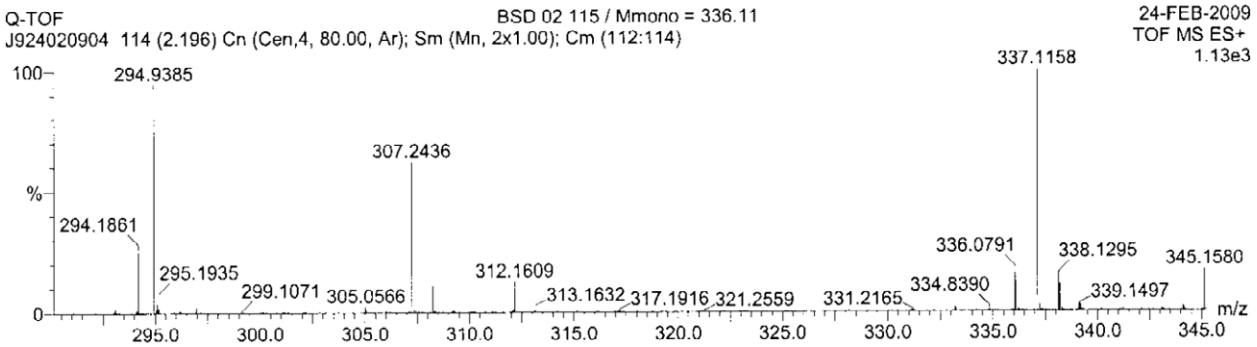
Elemental Composition Report

Page 1

Single Mass Analysis

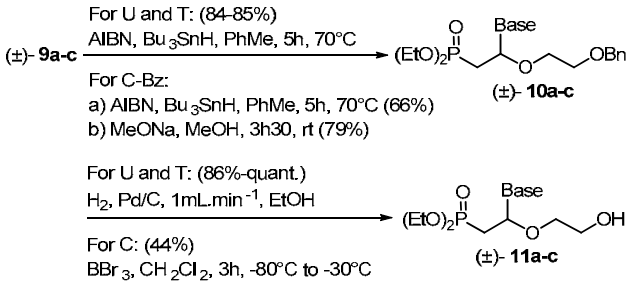
Tolerance = 3.0 mDa / DBE: min = -5.0, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
98 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

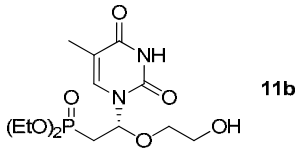


Minimum:				-5.0		
Maximum:		3.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
337.1158	337.1165	-0.7	-2.0	3.5	1	C12 H22 N2 O7 P
	337.1151	0.7	2.0	4.0	2	C10 H20 N5 O6 P
	337.1138	2.0	6.0	-1.0	3	C9 H24 N O10 P

II.10. *(±)*-Diethyl 2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11b

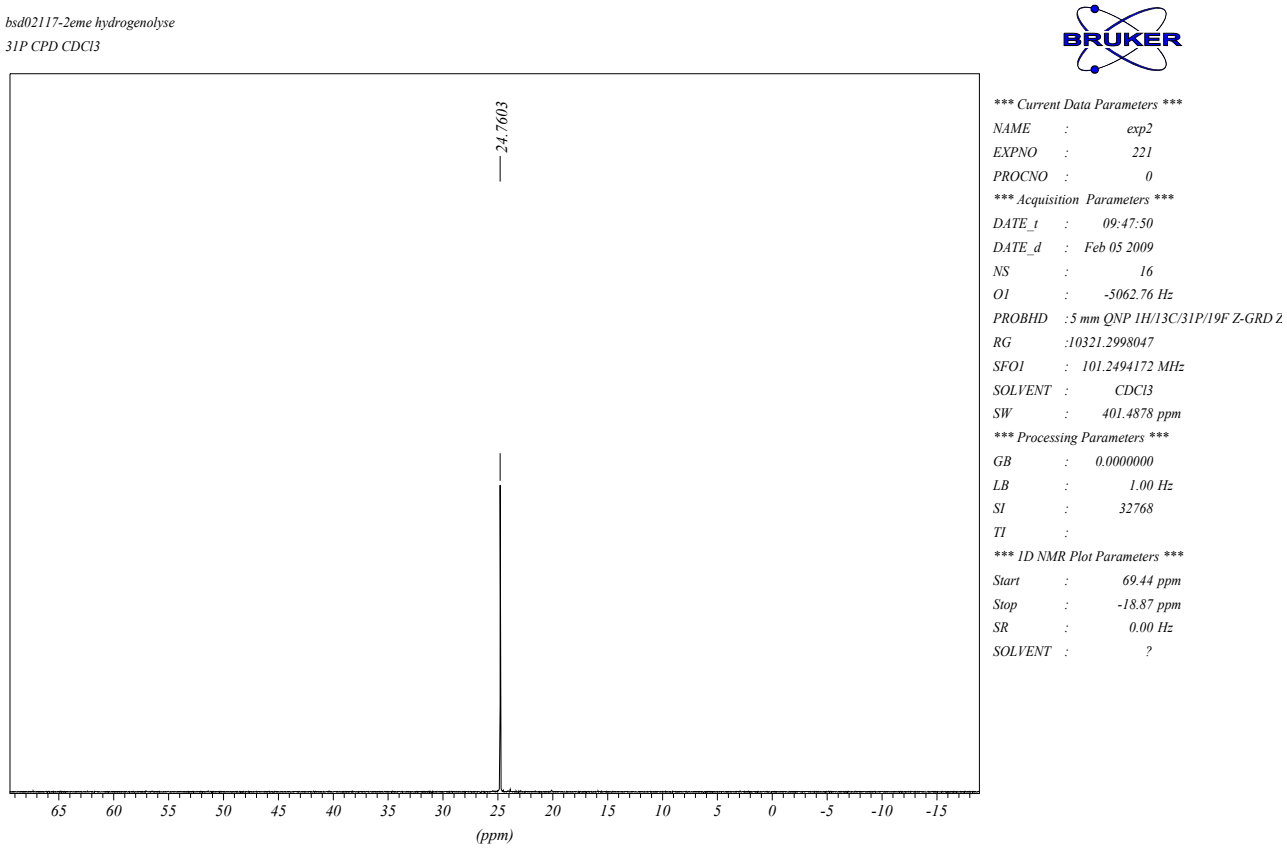


Scheme 3 Reduction and debenzylation steps

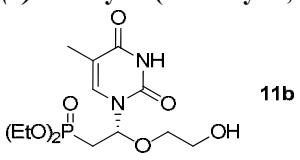


11b

$C_{13}H_{23}N_2O_7P$
MW = 350.31 g.mol^{-1}
Colorless oil (33 mg, 86 %)



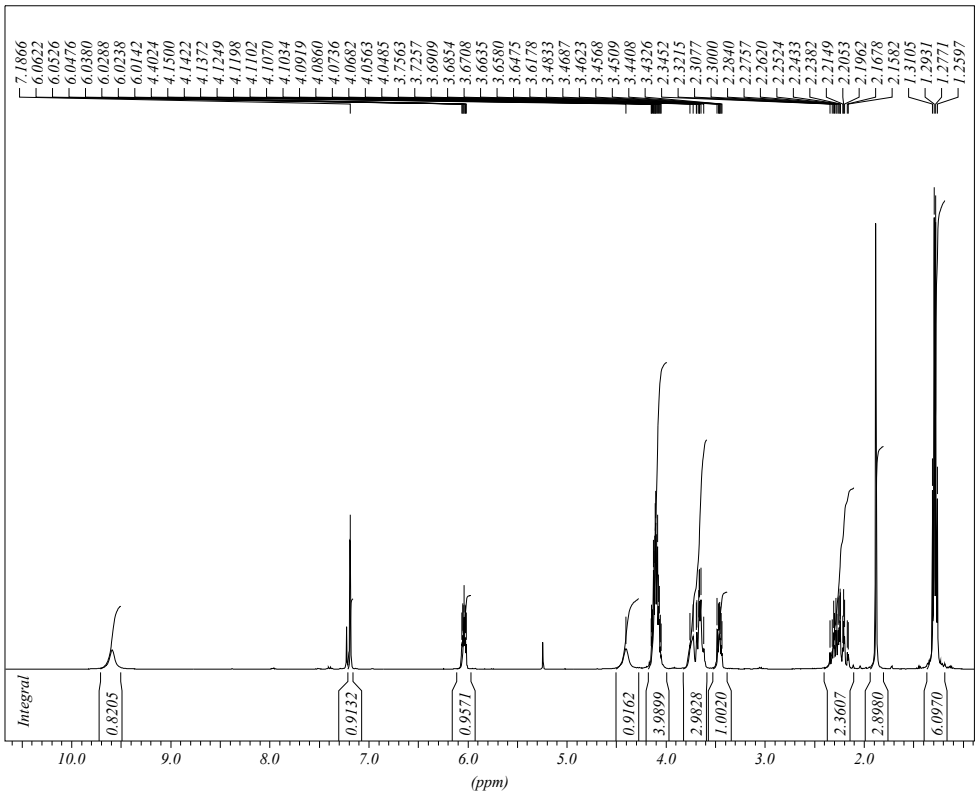
(±)-Diethyl 2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11b



11b

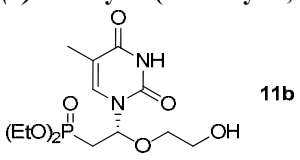
$C_{13}H_{23}N_2O_7P$
MW = 350.31 g.mol^{-1}
Colorless oil (33 mg, 86 %)

BSD 02 117-2PROTON CDCl3 opt/topspin cristau 29



*** Current Data Parameters ***
NAME : sech1
EXPNO : 202
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 03:45:15
DATE_d : Feb 13 2009
NS : 16
O1 : 2400.78 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG : 71.8000031
SFO1 : 400.1324008 MHz
SOLVENT : CDCl3
SW : 14.9831 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 10.67 ppm
Stop : 0.89 ppm
SR : 25.24 Hz
SOLVENT : ?

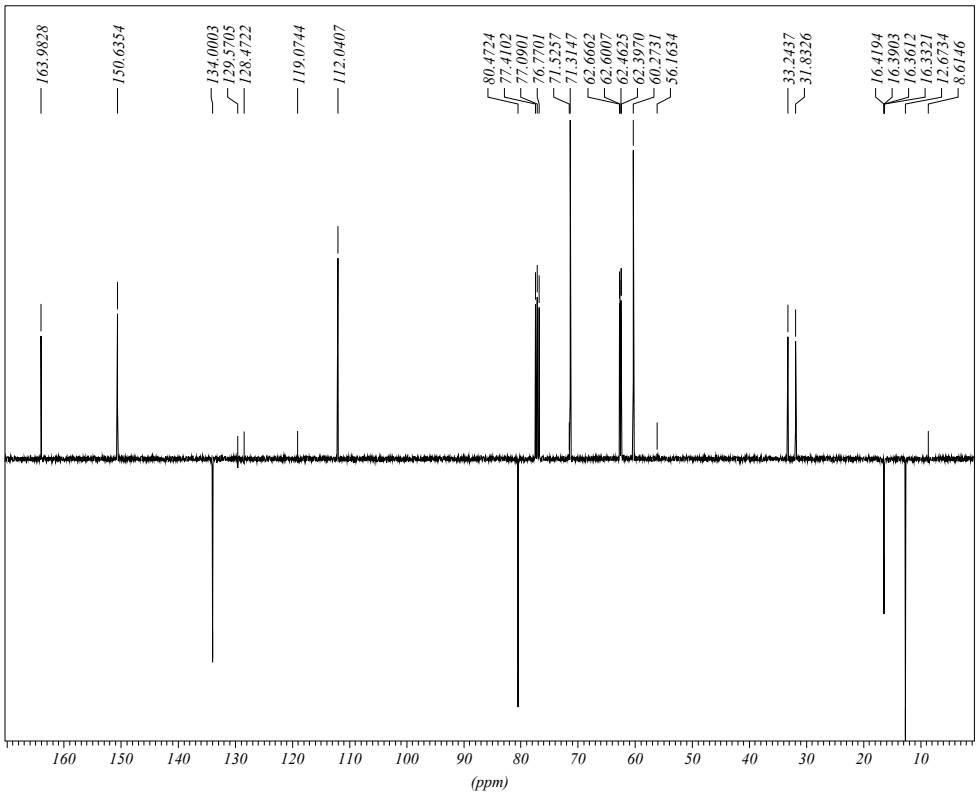
(±)-Diethyl 2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11b



11b

$C_{13}H_{23}N_2O_7P$
MW = 350.31 g.mol^{-1}
Colorless oil (33 mg, 86 %)

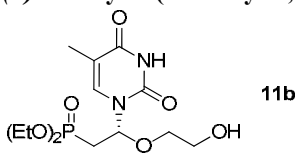
BSD 02 117C13APT CDCl3 opt/topspin cristau 15



BRUKER

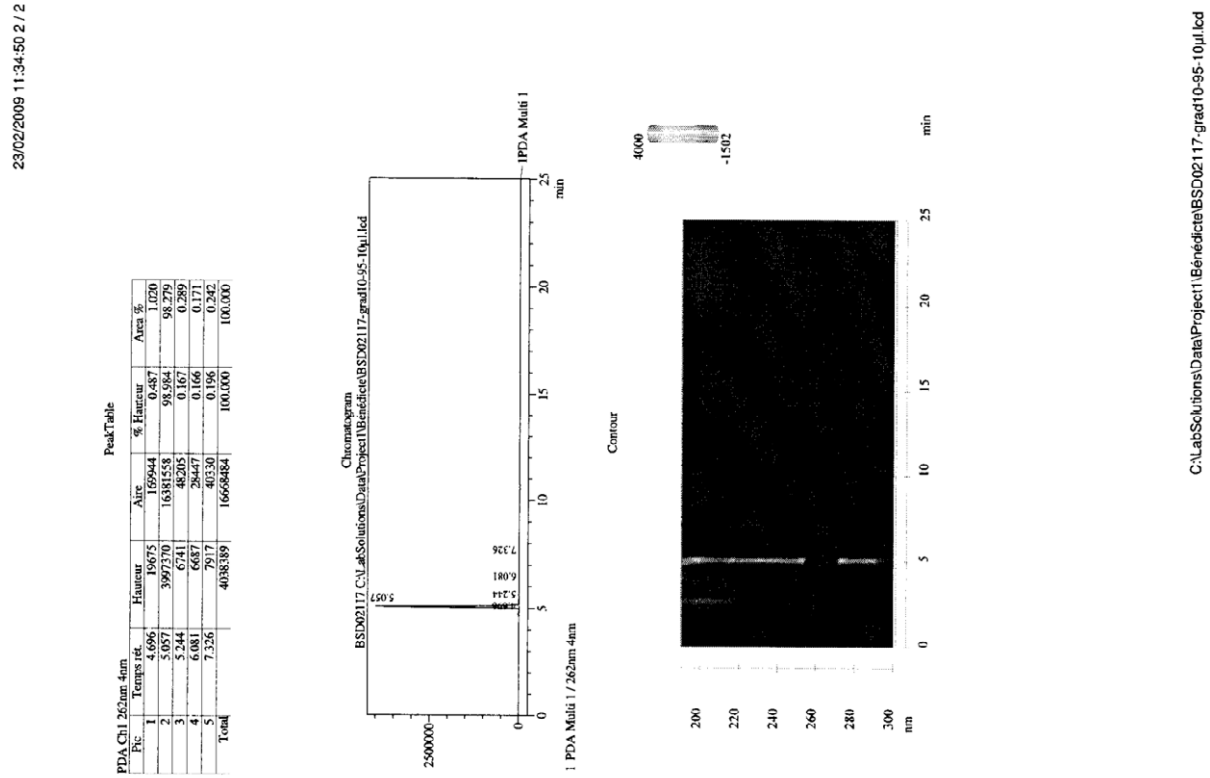
*** Current Data Parameters ***
NAME : 13C
EXPNO : 231
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 15:01:56
DATE_d : Feb 19 2009
NS : 1024
O1 : 10060.80 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG :16384.0000000
SFO1 : 100.6228298 MHz
SOLVENT : CDCl3
SW : 238.3238 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 170.37 ppm
Stop : 0.58 ppm
SR : 0.00 Hz
SOLVENT : ?

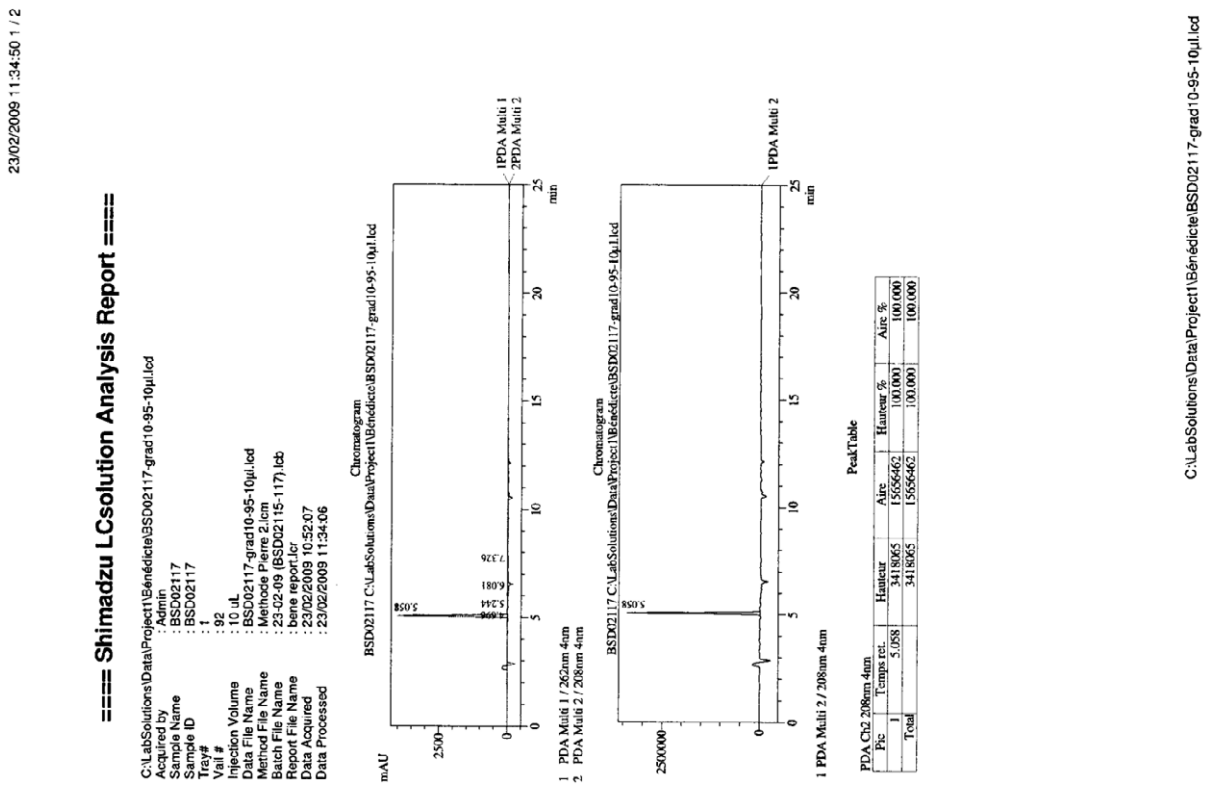
(±)-Diethyl 2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11b



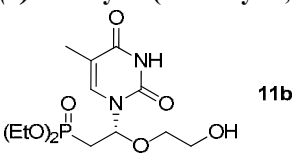
11b

$C_{13}H_{23}N_2O_7P$
MW = 350.31 g.mol^{-1}
Colorless oil (33 mg, 86 %)



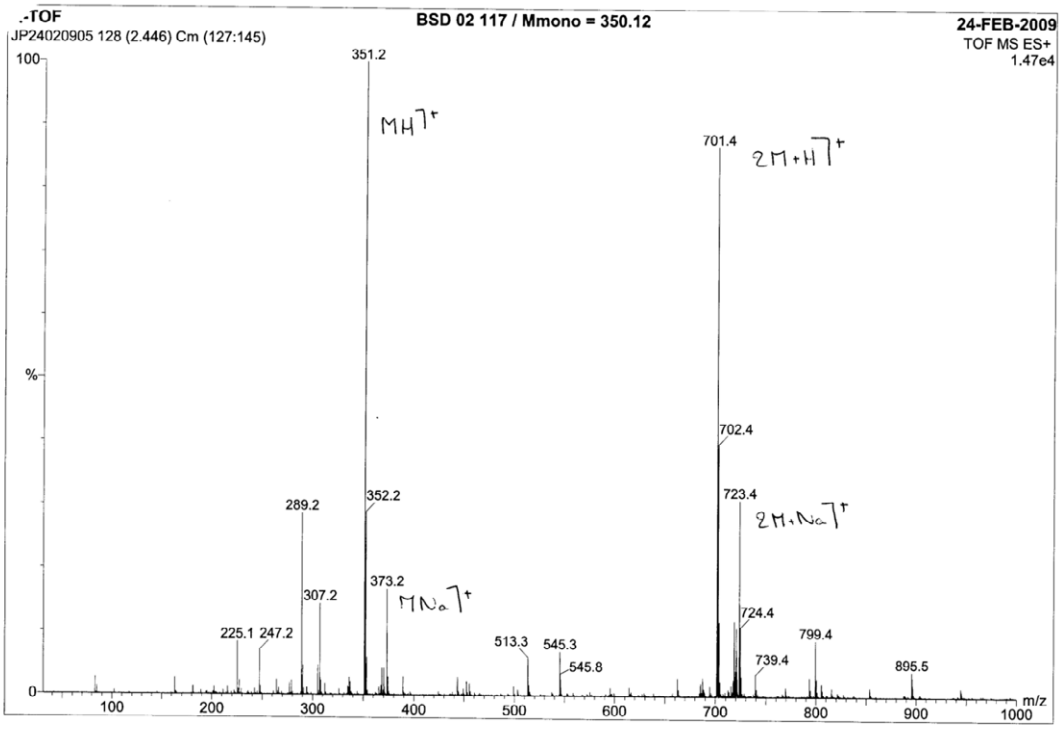


(±)-Diethyl 2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11b

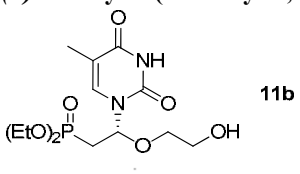


11b

$C_{13}H_{23}N_2O_7P$
MW = 350.31 g.mol^{-1}
Colorless oil (33 mg, 86 %)



***(±)*-Diethyl 2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11b**



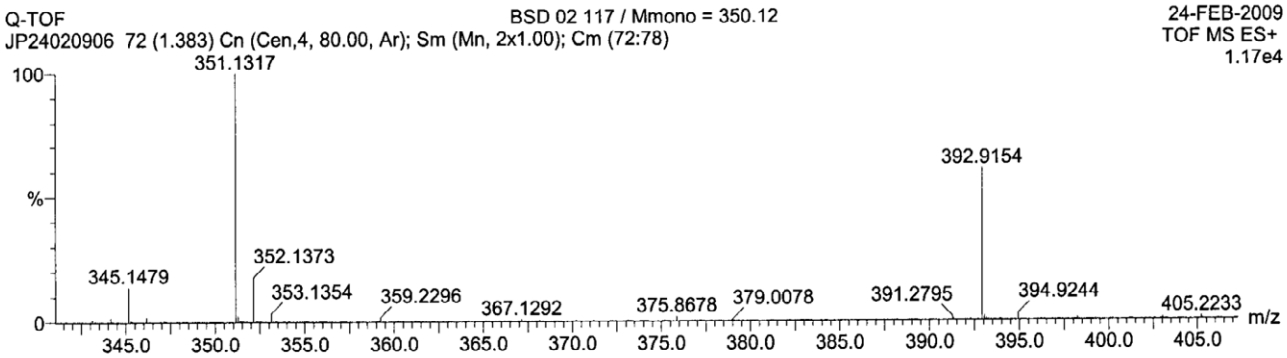
11b

$C_{13}H_{23}N_2O_7P$
MW = 350.31 g.mol^{-1}
Colorless oil (33 mg, 86 %)

Elemental Composition Report **Page 1**

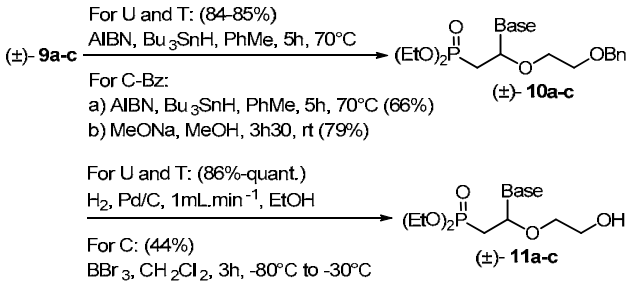
Single Mass Analysis
Tolerance = 3.0 mDa / DBE: min = -5.0, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
104 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)

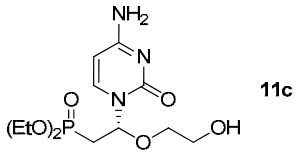


Minimum:				-5.0		
Maximum:		3.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
351.1317	351.1321	-0.4	-1.2	3.5	1	C13 H24 N2 O7 P
	351.1308	0.9	2.6	4.0	2	C11 H22 N5 O6 P
	351.1294	2.3	6.5	-1.0	3	C10 H26 N O10 P

II.11. (±)-Diethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11c

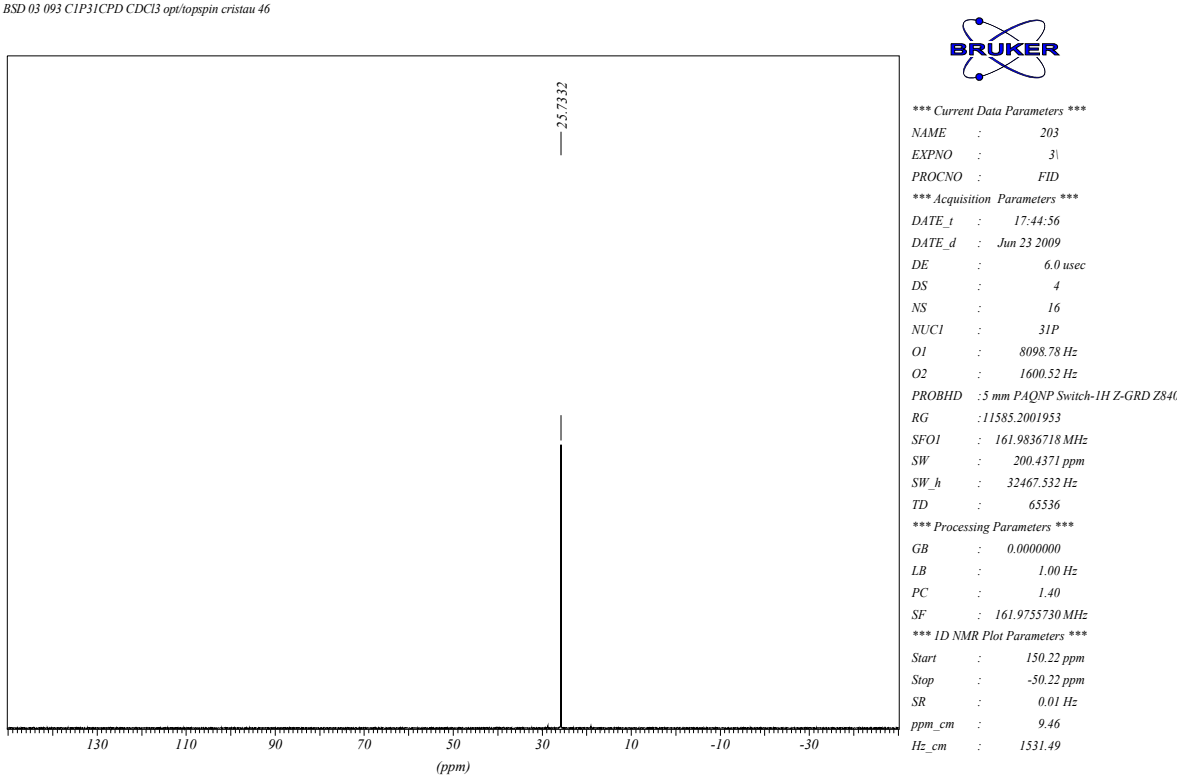


Scheme 3 Reduction and debenzylation steps

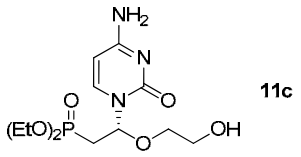


11c

$C_{12}H_{22}N_3O_6P$
MW = 335.36 g.mol^{-1}
Colorless oil (35 mg, 37 %)

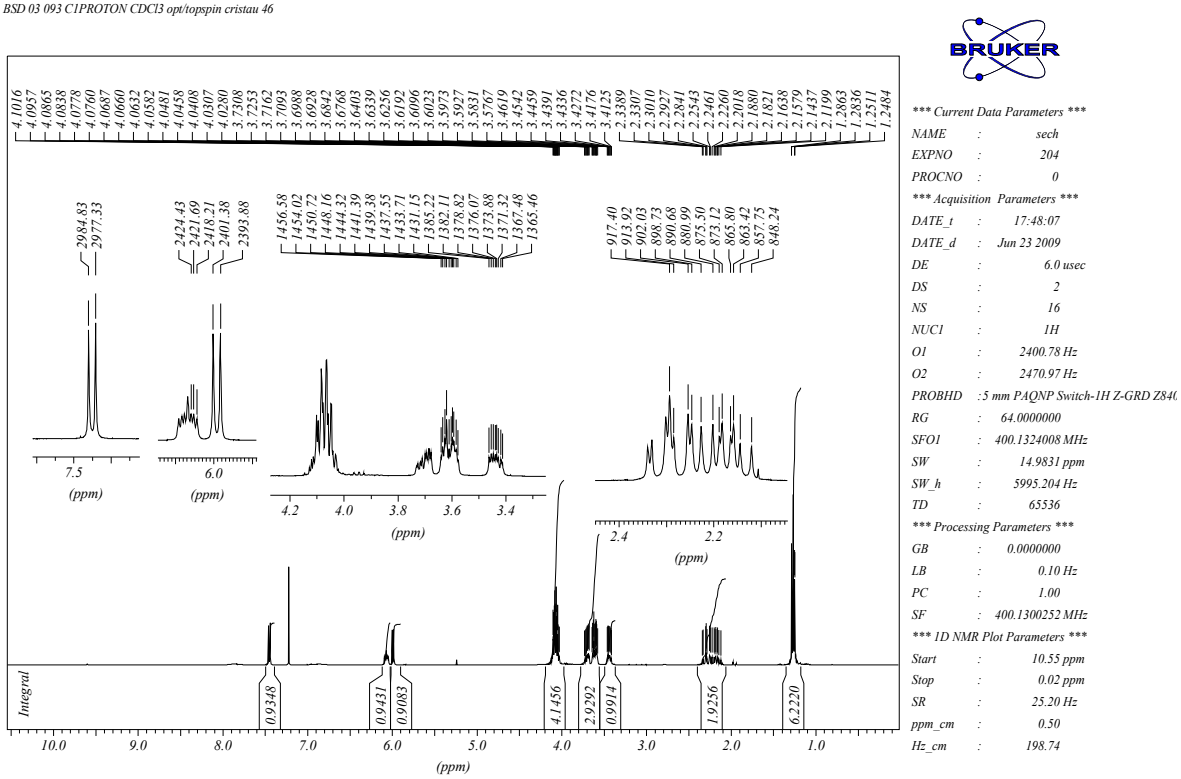


(±)-Diethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11c

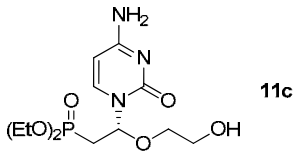


11c

$C_{12}H_{22}N_3O_6P$
MW = 335.36 g.mol^{-1}
Colorless oil (35 mg, 37 %)

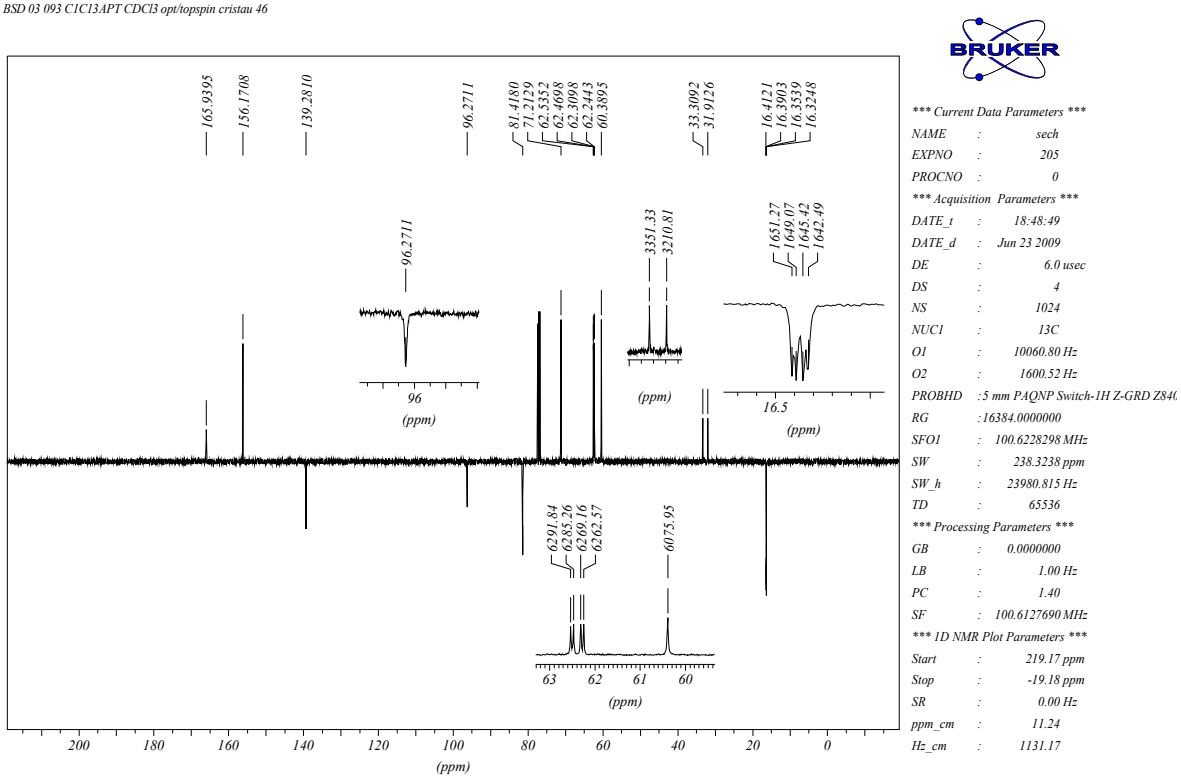


(±)-Diethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11c

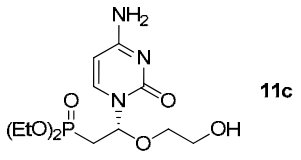


11c

$C_{12}H_{22}N_3O_6P$
MW = 335.36 g.mol^{-1}
Colorless oil (35 mg, 37 %)



(±)-Diethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11c



11c

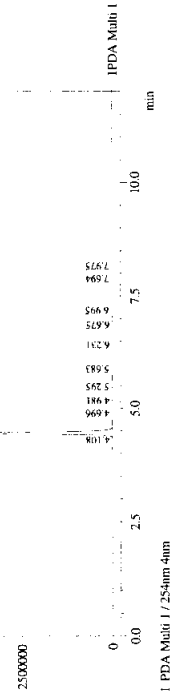
$C_{12}H_{22}N_3O_6P$
MW = 335.36 g.mol^{-1}
Colorless oil (35 mg, 37 %)

01/07/2009 15:23:42 3

PDA Ch1 254nm 4nm PeakTable

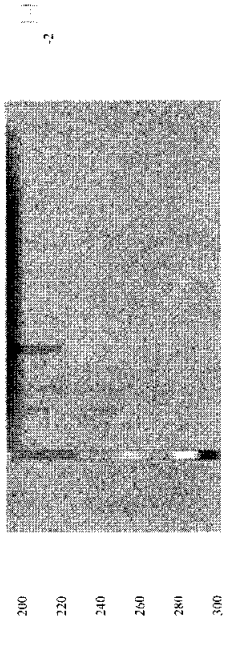
Pic	Temps ret.	Hauteur	Aire	% Hauteur	Aire %
1	4.108	2517	13375	0.062	0.092
2	4.448	3995832	14209262	98.459	97.395
3	4.696	10605	46604	0.261	0.319
4	4.981	5913	27356	0.146	0.188
5	5.295	4958	36705	0.122	0.252
6	5.683	10091	80747	0.249	0.553
7	6.231	2020	9104	0.050	0.062
8	6.675	1678	8058	0.041	0.055
9	6.995	17900	127447	0.441	0.874
10	7.694	1773	11811	0.044	0.081
11	7.975	3424	18908	0.084	0.130
Total		4056712	14589380	100.000	100.000

Chromatogram
BSD03 093 C1 C:\LabSolutions\Data\Project1\Bénédicte\BSD 03 093 C1 - 10µl.lcd



1 PDA Multi 1 / 254nm 4nm

Contour



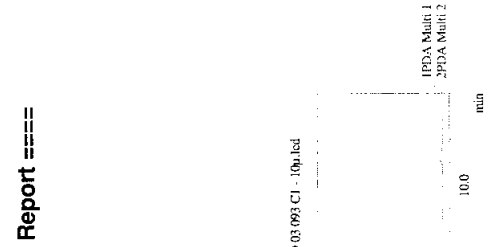
C:\LabSolutions\Data\Project1\Bénédicte\BSD 03 093 C1 - 10µl

01/07/2009 15:23:42 1

==== Shimadzu LCsolution Analysis Report ====

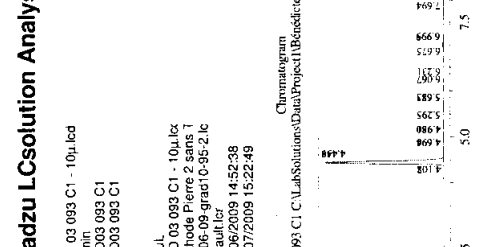
C:\...\Project1\Bénédicte\BSD 03 093 C1 - 10µl.lcd	
Acquired by	: Admin
Sample Name	: BSD03 093 C1
Sample ID	: BSD03 093 C1
Tray#	: 1
Vial #	: 98
Injection Volume	: 10 uL
Data File Name	: BSD 03 093 C1 - 10µl.lcx
Method File Name	: Methode Pierre 2 sans T
Batch File Name	: 26-06-09-grad10-95-2.lc
Report File Name	: Default.lcr
Data Acquired	: 26/06/2009 14:52:38
Data Processed	: 01/07/2009 15:22:49

Chromatogram
BSD03 093 C1 C:\LabSolutions\Data\Project1\Bénédicte\BSD 03 093 C1 - 10µl.lcd



1 PDA Multi 1 / 254nm 4nm
2 PDA Multi 2 / 210nm 4nm

Chromatogram
BSD03 093 C1 C:\LabSolutions\Data\Project1\Bénédicte\BSD 03 093 C1 - 10µl.lcd



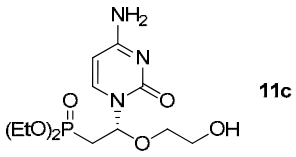
1 PDA Multi 2 / 210nm 4nm

PDA Ch2 210nm 4nm PeakTable

Pic	Temps ret.	Hauteur	Aire	Hauteur %	Aire %
1	4.107	4181	19865	0.101	0.101
2	4.459	3995837	18667404	96.579	95.347
3	4.694	24540	135037	0.593	0.690
4	4.980	13105	62490	0.317	0.319
5	5.295	10763	74375	0.260	0.380
6	5.675	14933	119044	0.361	0.608
7	6.067	7076	34613	0.171	0.177
8	6.999	26309	195910	0.636	1.001
9	7.972	6126	73384	0.148	0.375
10	8.312	34520	196301	0.834	1.003
Total		4137390	19578423	100.000	100.000

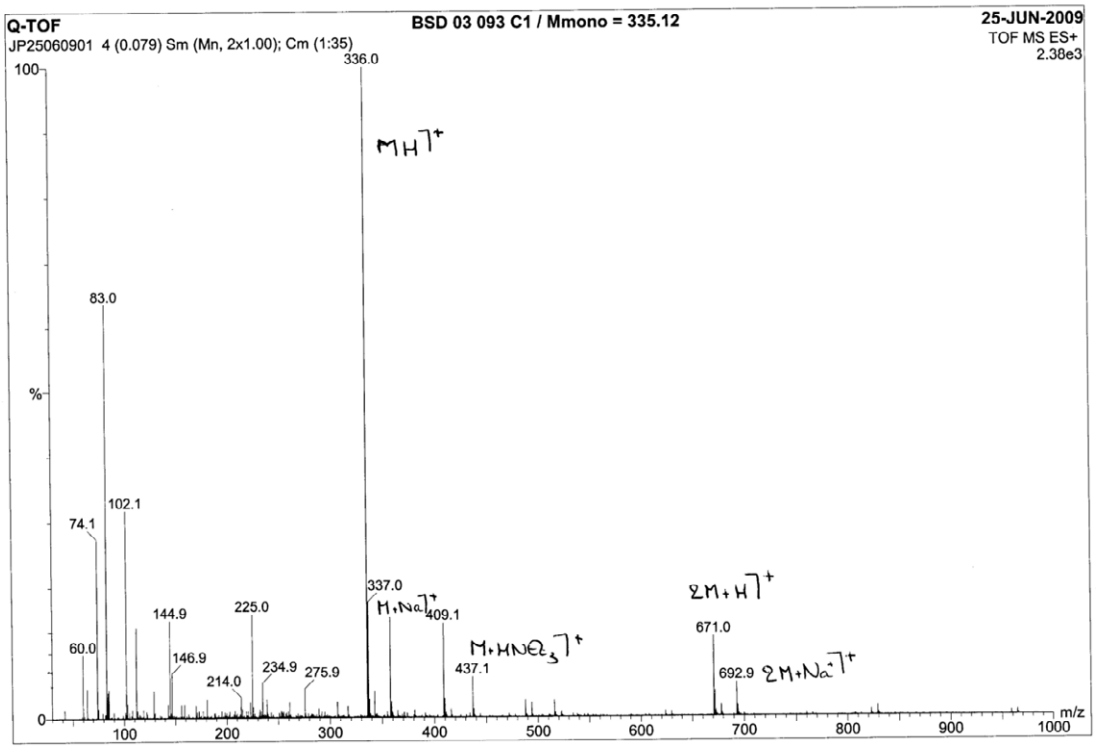
C:\LabSolutions\Data\Project1\Bénédicte\BSD 03 093 C1 - 10µl

(±)-Diethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11c

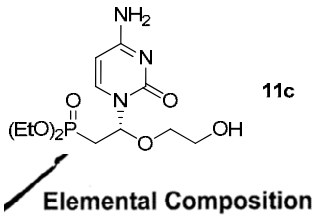


11c

$C_{12}H_{22}N_3O_6P$
MW = 335.36 g.mol^{-1}
Colorless oil (35 mg, 37 %)



(±)-Diethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 11c



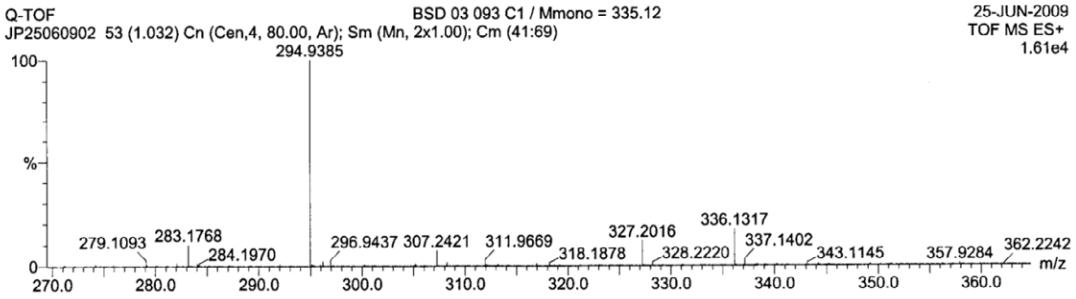
11c

$C_{12}H_{22}N_3O_6P$
MW = 335.36 g.mol^{-1}
Colorless oil (35 mg, 37 %)

Elemental Composition Report **Page 1**

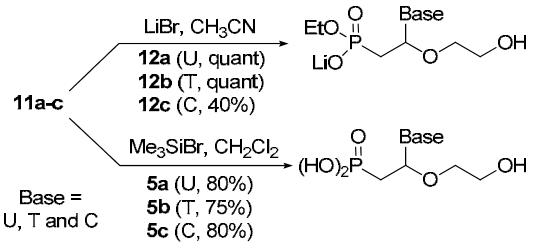
Single Mass Analysis
Tolerance = 3.0 mDa / DBE: min = -10.0, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
189 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)

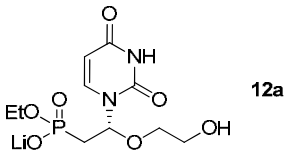


Minimum:				-10.0		
Maximum:		3.0	5.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
336.1317	336.1324	-0.7	-2.2	3.5	1	C12 H23 N3 O6 P ←
	336.1298	1.9	5.7	-1.0	2	C9 H25 N2 O9 P

II.12. *(±)*-Lithium ethyl 2-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate **12a**

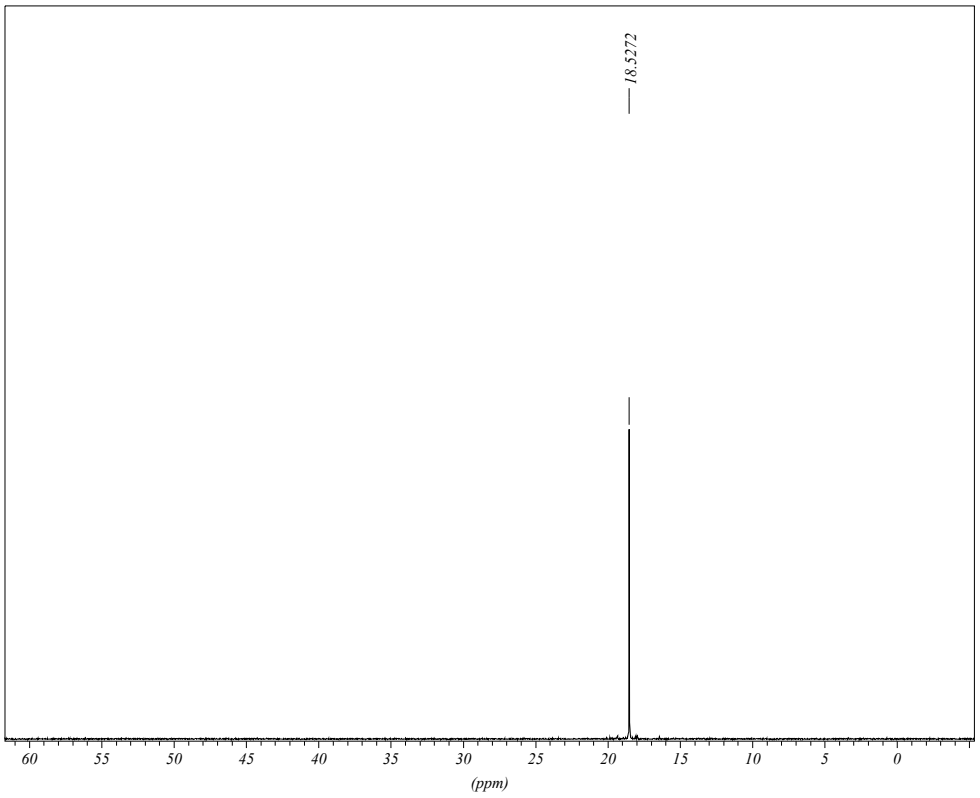


Scheme 4 Synthesis of free phosphonic acid and mono-lithium salt derivatives **5a**-c and **12a-c**



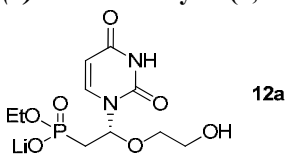
$C_{10}H_{16}N_2O_7PLi$
MW = 314.17 g.mol^{-1}
White solid (15 mg, 76%)

BSD 03 017P31CPD D2O opt/topspin cristau 38



*** Current Data Parameters ***
NAME : brut
EXPNO : 210
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 05:13:41
DATE_d : Mar 23 2009
NS : 16
O1 : 8098.78 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z84(
RG :20642.5000000
SFO1 : 161.9836718 MHz
SOLVENT : D2O
SW : 200.4371 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 61.70 ppm
Stop : -5.34 ppm
SR : 0.01 Hz
SOLVENT : ?

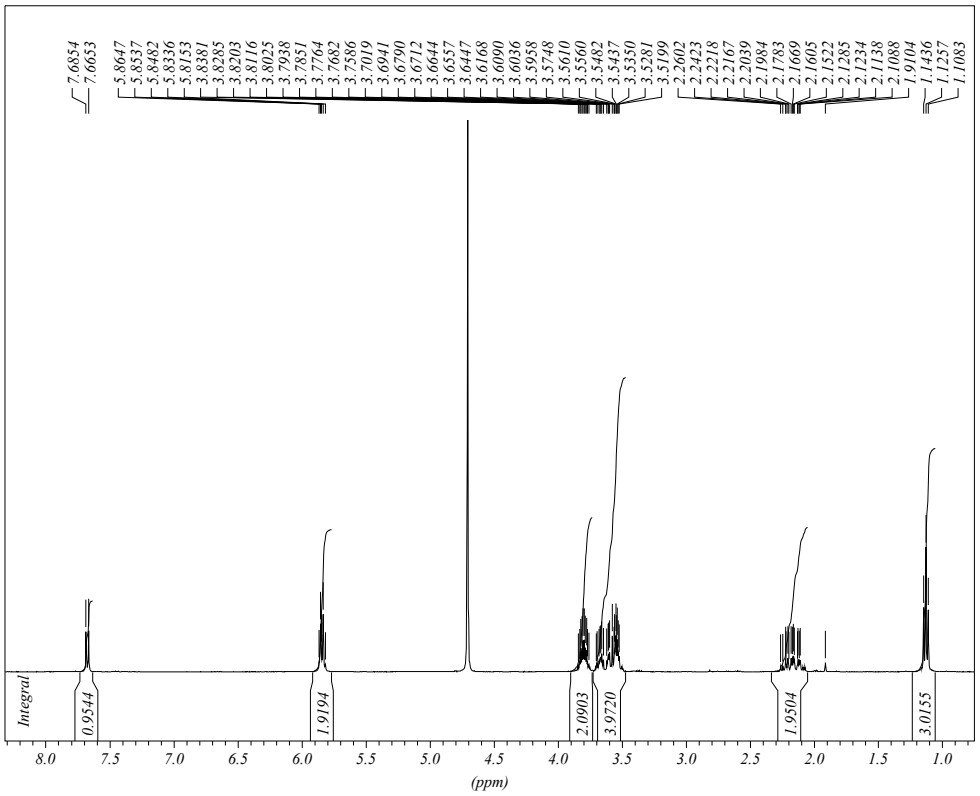
(±)-Lithium ethyl 2-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 12a



12a

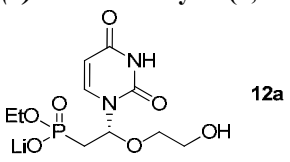
$C_{10}H_{16}N_2O_7PLi$
MW = 314.17 g.mol^{-1}
White solid (15 mg, 76%)

BSD 03 017PROTON D2O opt/topspin cristau 38



*** Current Data Parameters ***
NAME : brut
EXPNO : 211
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 05:17:20
DATE_d : Mar 23 2009
NS : 16
O1 : 2400.78 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG : 114.0000000
SFO1 : 400.1324008 MHz
SOLVENT : D2O
SW : 14.9831 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 8.32 ppm
Stop : 0.75 ppm
SR : -0.00 Hz
SOLVENT : ?

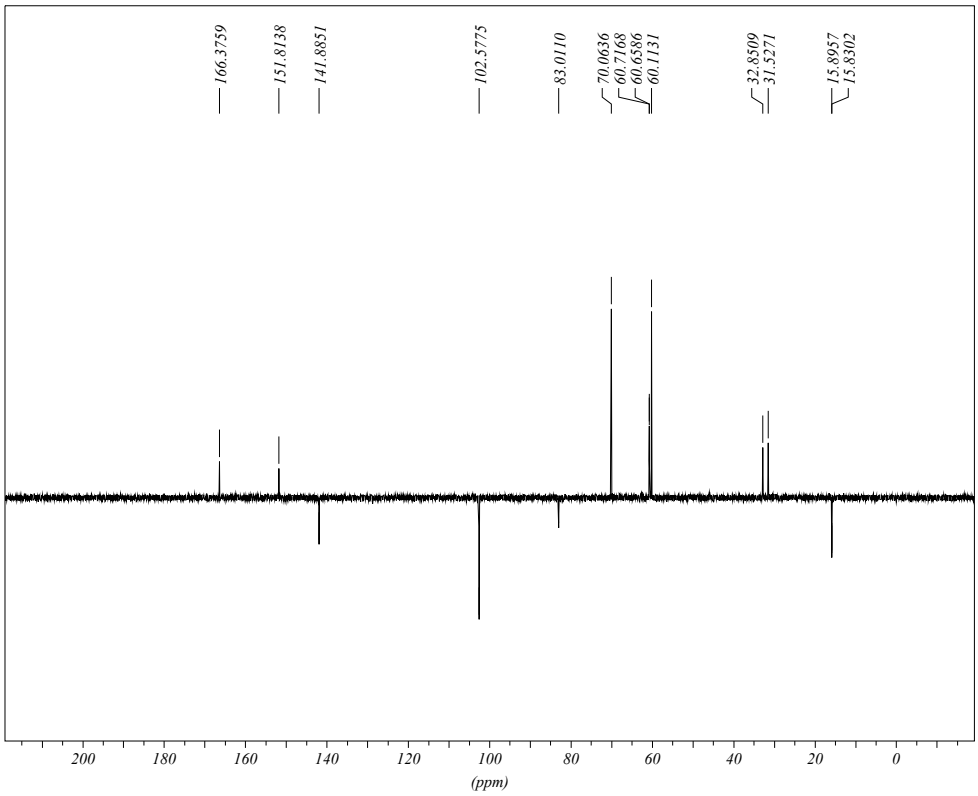
(±)-Lithium ethyl 2-(2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 12a



12a

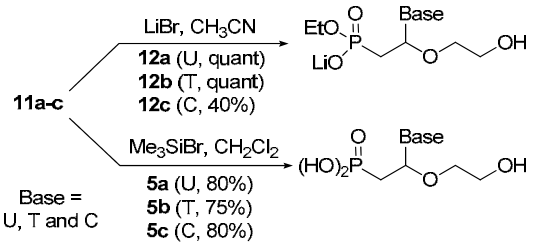
$C_{10}H_{16}N_2O_7PLi$
MW = 314.17 g.mol^{-1}
White solid (15 mg, 76%)

BSD 03 017C13APT D2O opt/topspin cristau 37

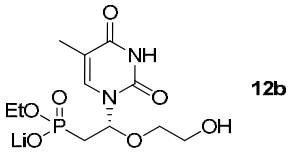


*** Current Data Parameters ***
NAME : brut
EXPNO : 212
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 11:05:55
DATE_d : Mar 24 2009
NS : 1024
O1 : 10060.80 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z840
RG :26008.0000000
SFO1 : 100.6228298 MHz
SOLVENT : D2O
SW : 238.3238 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 219.17 ppm
Stop : -19.18 ppm
SR : 0.00 Hz
SOLVENT : ?

II.13. *(±)*-Lithium ethyl 2-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 12b



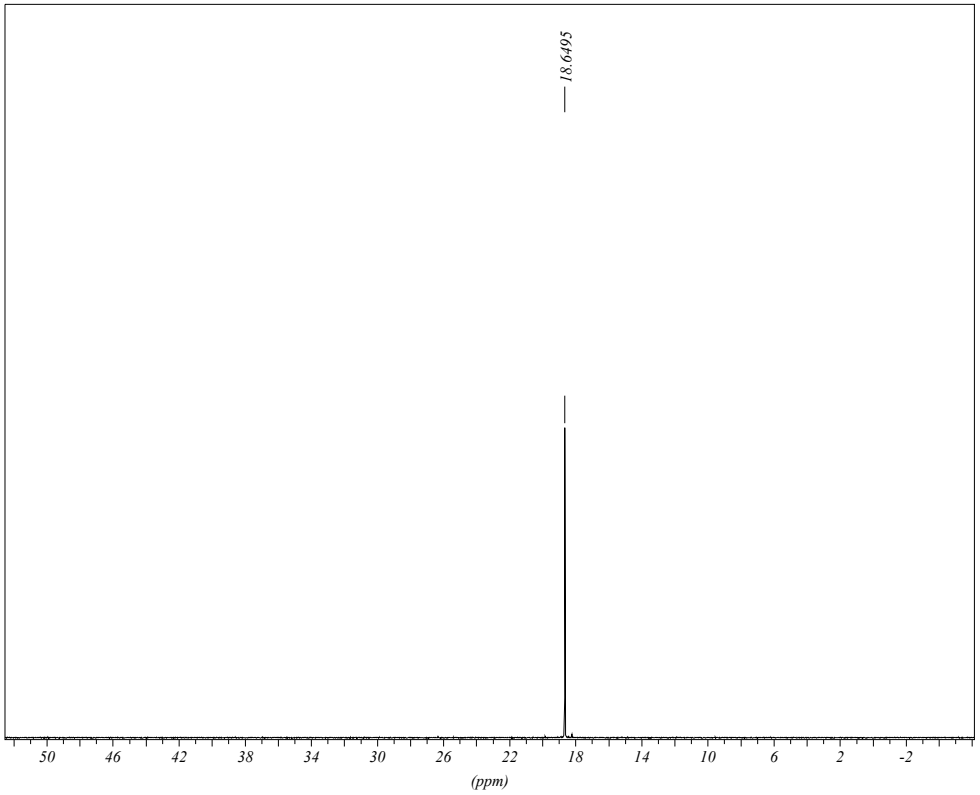
Scheme 4 Synthesis of free phosphonic acid and mono-lithium salt derivatives **5a**-c and **12a-c**



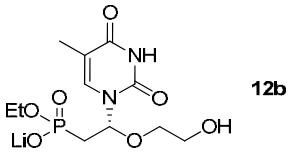
12b

$C_{11}H_{18}N_2O_7PLi$
MW = 328.19 g.mol^{-1}
White solid (20 mg, 85%)

BSD 03 021P31CPD D2O opt/topspin cristau 57

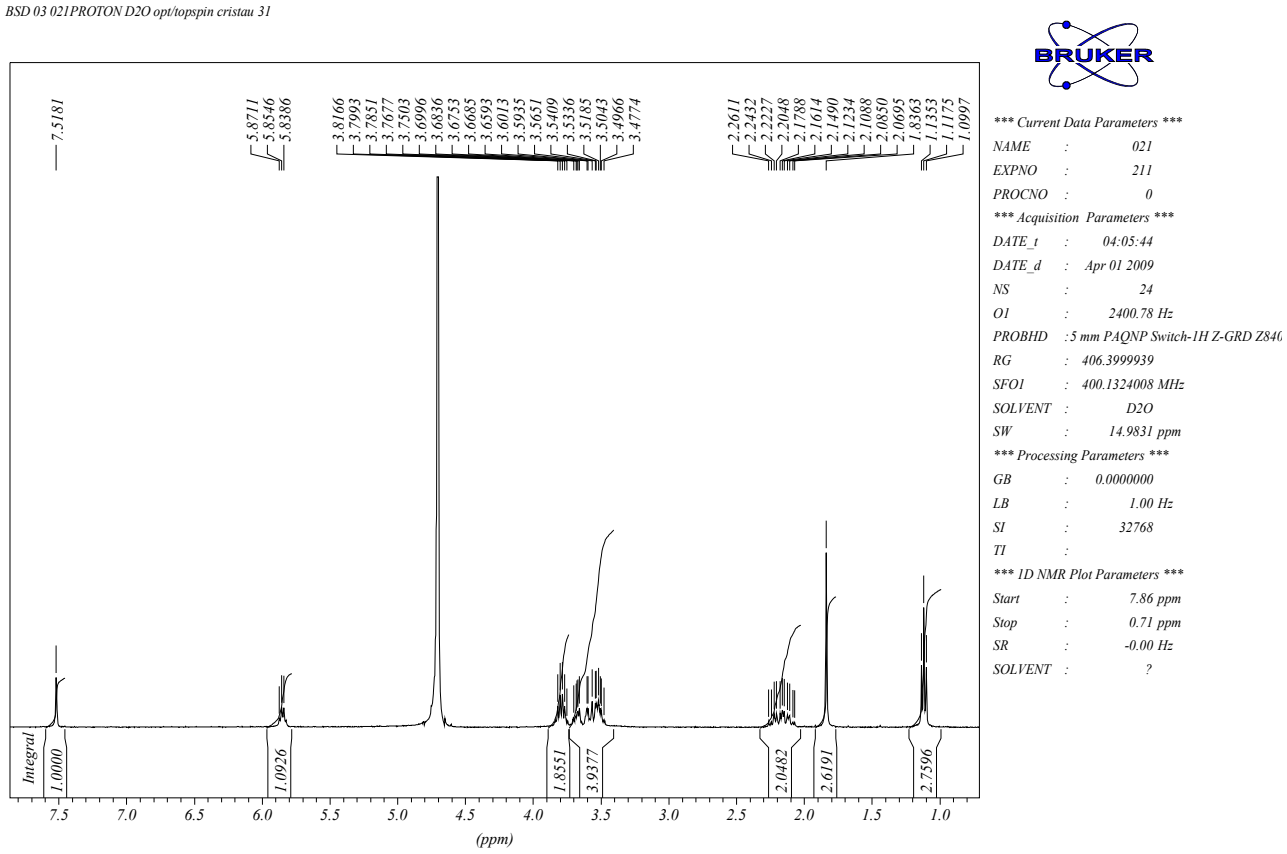


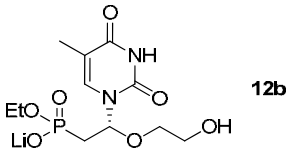
*** Current Data Parameters ***
NAME : conc
EXPNO : 210
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 05:33:49
DATE_d : Apr 07 2009
NS : 16
O1 : 8098.78 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-GRD Z840
RG :20642.5000000
SFO1 : 161.9836718 MHz
SOLVENT : D2O
SW : 200.4371 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 52.54 ppm
Stop : -6.13 ppm
SR : 0.01 Hz
SOLVENT : ?



12b

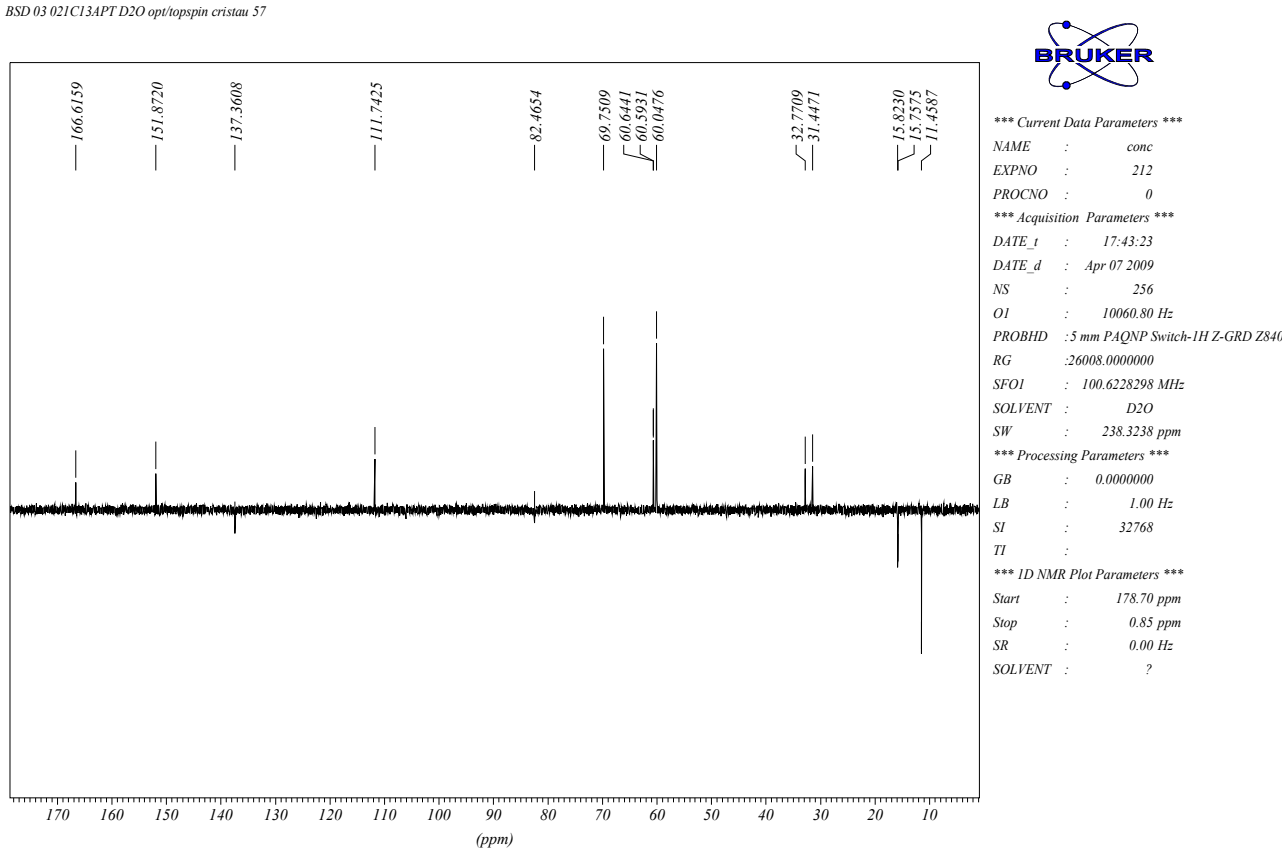
$C_{11}H_{18}N_2O_7PLi$
MW = 328.19 g.mol^{-1}
White solid (20 mg, 85%)



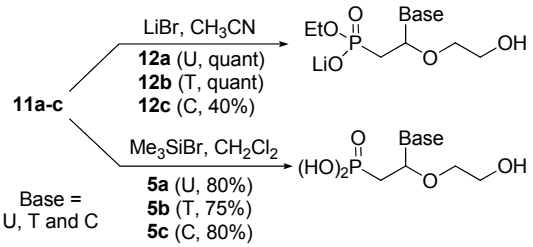


12b

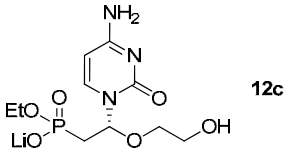
$C_{11}H_{18}N_2O_7PLi$
MW = 328.19 g.mol^{-1}
White solid (20 mg, 85%)



II.14. *(±)*-Lithium ethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 12c



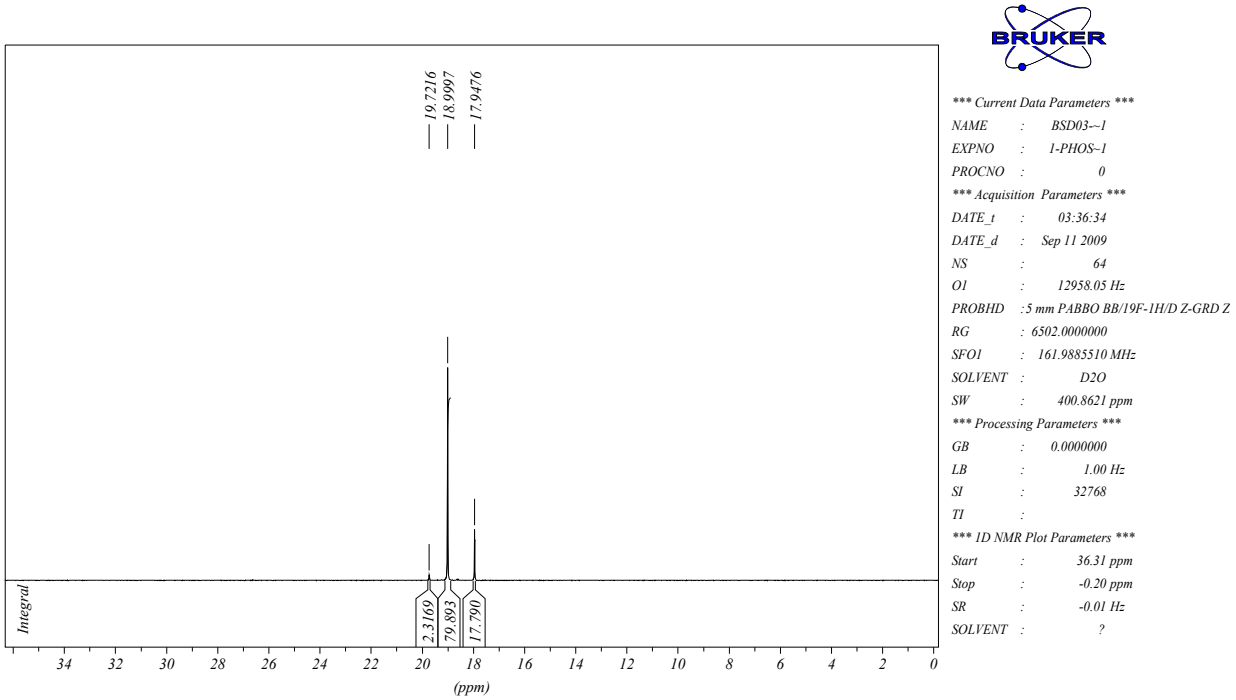
Scheme 4 Synthesis of free phosphonic acid and mono-lithium salt derivatives **5a**-c and **12a-c**



12c

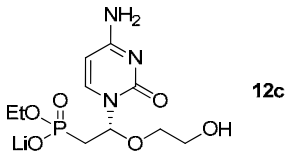
$C_{10}H_{17}N_3O_6PLi$
MW = 309.36 g.mol^{-1}
80% pure by phosphorus NMR

BSDO3-121 / D2O



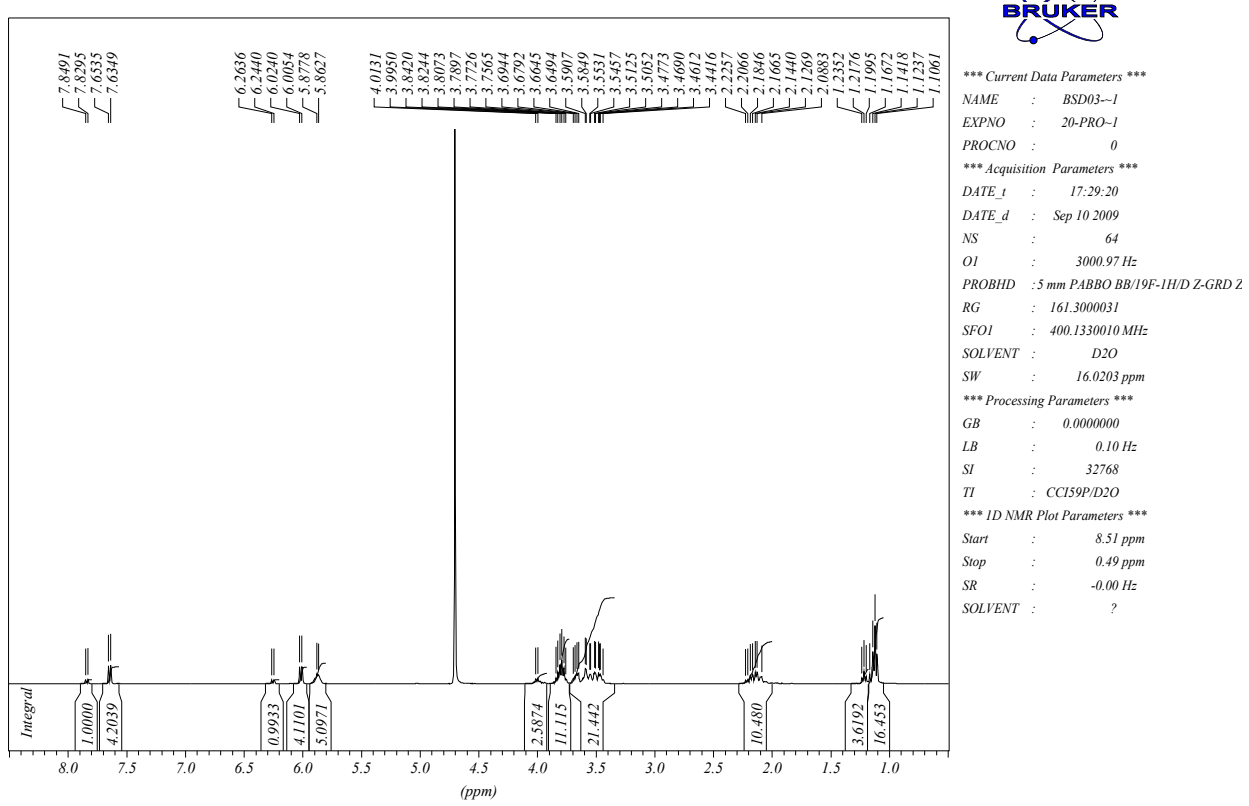
*** Current Data Parameters ***
NAME : BSD03-~1
EXPNO : 1-PHOS~1
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 03:36:34
DATE_d : Sep 11 2009
NS : 64
O1 : 12958.05 Hz
PROBHD : 5 mm PABBO BB/19F-1H/D Z-GRD Z
RG : 6502.0000000
SFO1 : 161.9885510 MHz
SOLVENT : D2O
SW : 400.8621 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 36.31 ppm
Stop : -0.20 ppm
SR : -0.01 Hz
SOLVENT : ?

(±)-Lithium ethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 12c



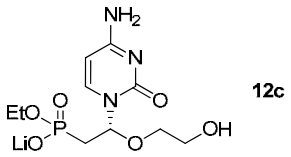
12c

$C_{10}H_{17}N_3O_6PLi$
MW = 309.36 g.mol^{-1}
80% pure by phosphorus NMR



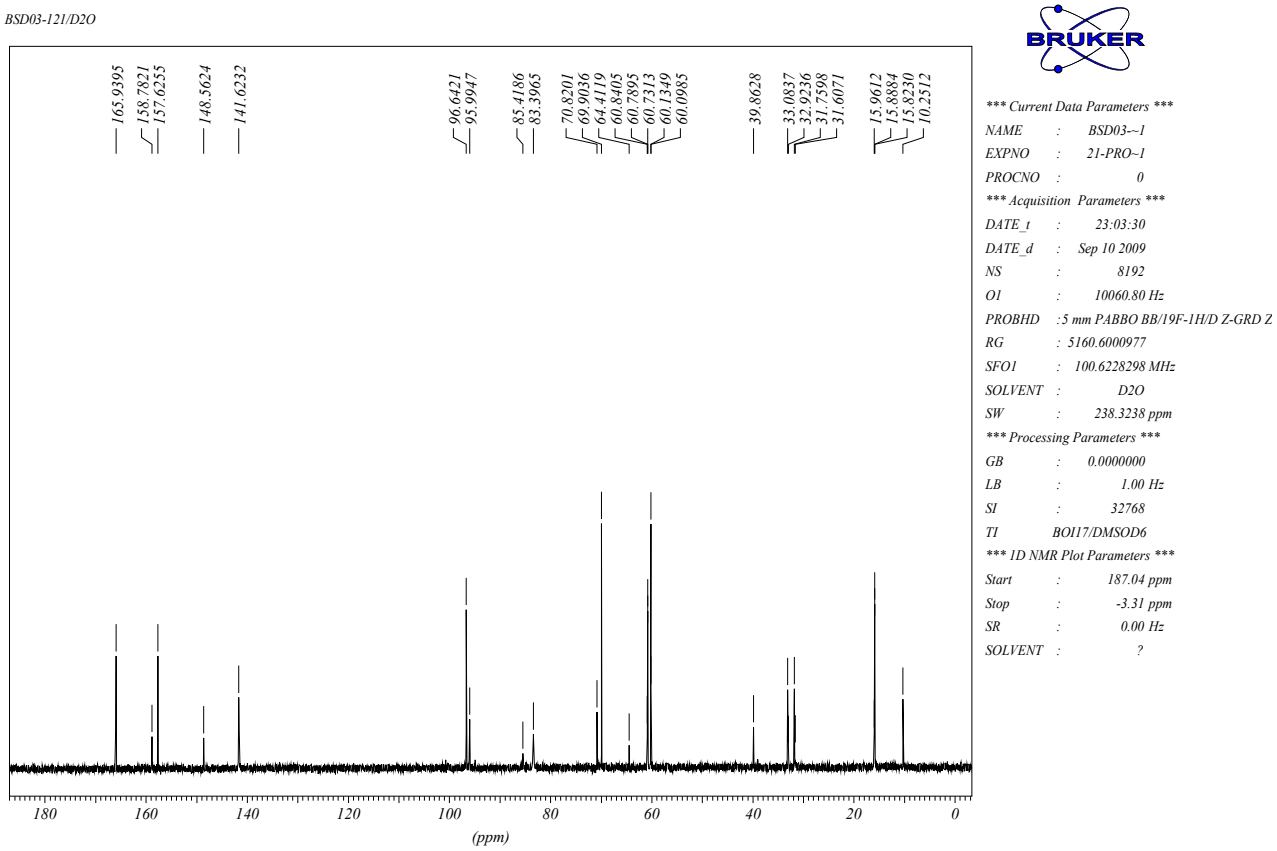
*** Current Data Parameters ***
NAME : BSD03-~1
EXPNO : 20-PRO~1
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 17:29:20
DATE_d : Sep 10 2009
NS : 64
O1 : 3000.97 Hz
PROBHD : 5 mm PABBO BB/19F-1H/D Z-GRD Z
RG : 161.3000031
SFO1 : 400.1330010 MHz
SOLVENT : D2O
SW : 16.0203 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 0.10 Hz
SI : 32768
TI : CCI59P/D2O
*** 1D NMR Plot Parameters ***
Start : 8.51 ppm
Stop : 0.49 ppm
SR : -0.00 Hz
SOLVENT : ?

(±)-Lithium ethyl 2-(4-amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonate 12c

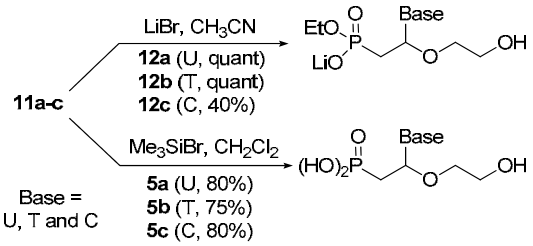


12c

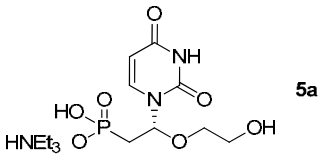
$C_{10}H_{17}N_3O_6PLi$
MW = 309.36 g.mol^{-1}
80% pure by phosphorus NMR



II.15. *(±)*-2-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonic acid triethyl ammonium salt 5a



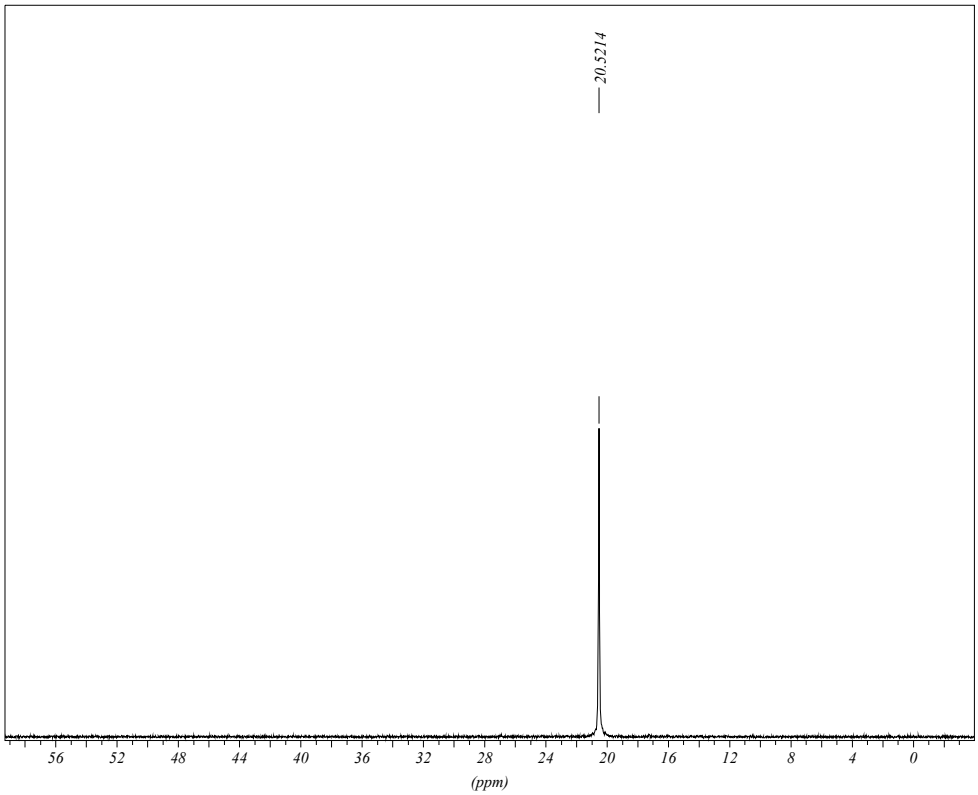
Scheme 4 Synthesis of free phosphonic acid and mono-lithium salt derivatives **5a**-c and **12a-c**



5a

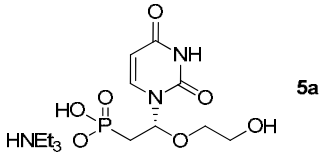
$C_8H_{13}N_2O_7P$ phosphonic diacid form
$C_{14}H_{27}N_3O_7P$ triethylammonium salt
$MW_{diacid\ form}$ = 280.18 g.mol^{-1}
$MW_{ammonium\ salt}$ = 380.37 g.mol^{-1}
Ammonium salt is a colorless oil (60 mg, 32 %)

BSD 03 045 C18 F1P31CPD D2O opt/topspin cristau 59



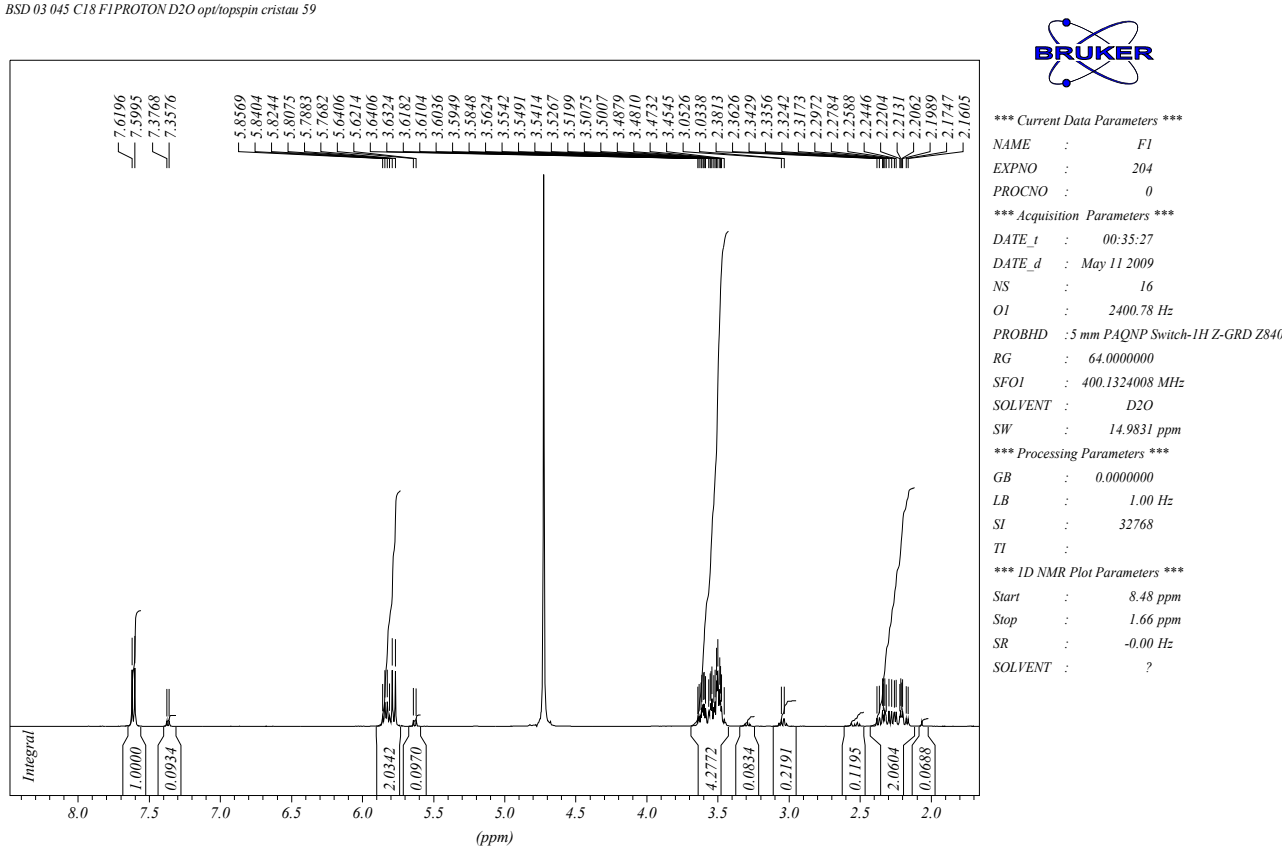
*** Current Data Parameters ***
NAME : F1
EXPNO : 203
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 00:32:02
DATE_d : May 11 2009
NS : 16
O1 : 8098.78 Hz
PROBHD :5 mm PAQNP Switch-1H Z-GRD Z84(
RG :11585.2001953
SFO1 : 161.9836718 MHz
SOLVENT : D2O
SW : 200.4371 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 59.33 ppm
Stop : -3.98 ppm
SR : 0.01 Hz
SOLVENT : ?

(±)-2-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonic acid triethylammonium salt 5a

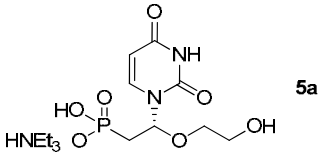


5a

$C_8H_{13}N_2O_7P$ phosphonic diacid form
$C_{14}H_{27}N_3O_7P$ triethylammonium salt
$MW_{diacid\ form}$ = 280.18 g.mol^{-1}
$MW_{ammonium\ salt}$ = 380.37 g.mol^{-1}
Ammonium salt is a colorless oil (60 mg, 32 %)

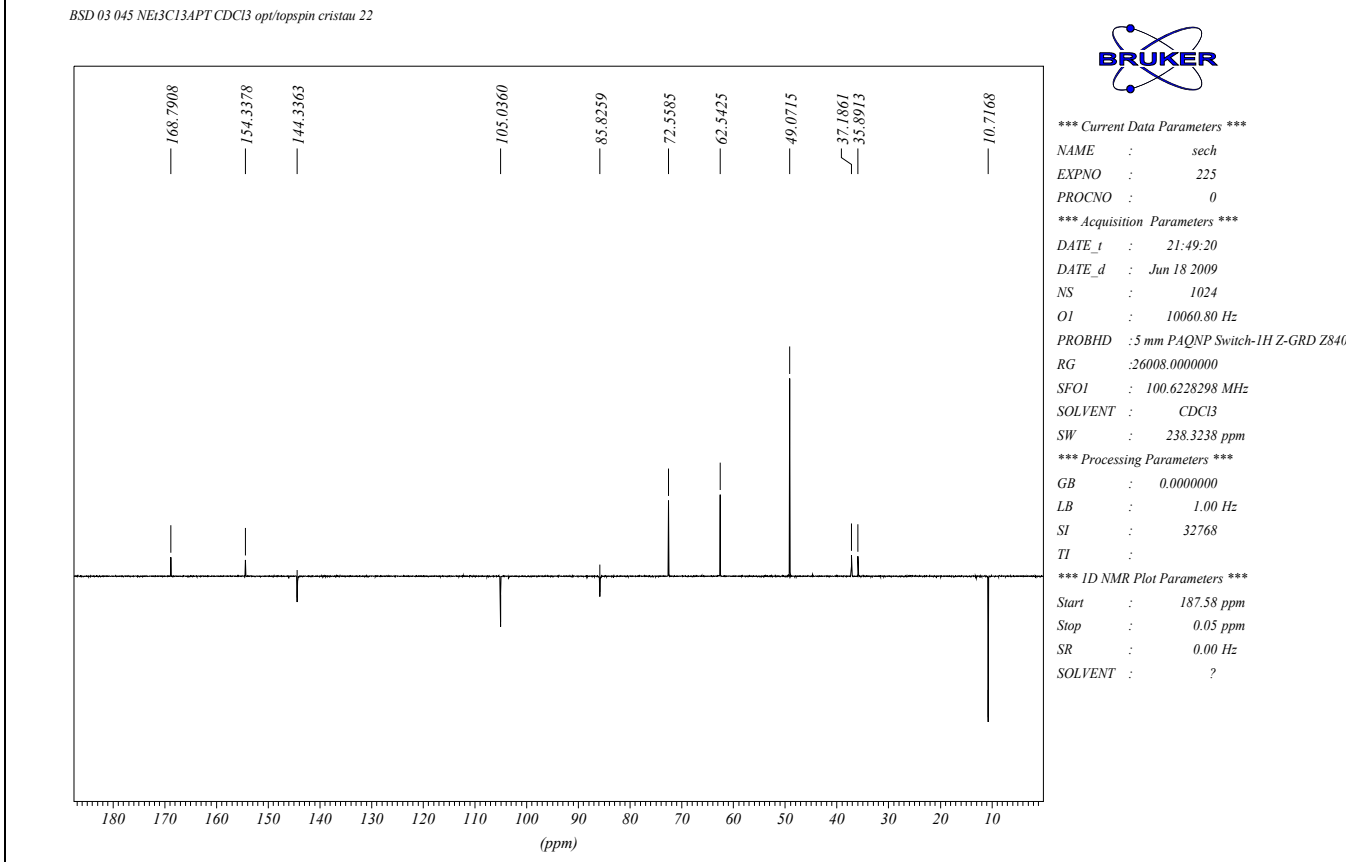


(±)-2-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonic acid triethylammonium salt 5a

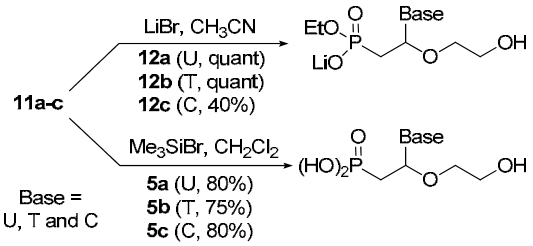


5a

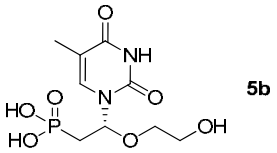
$C_8H_{13}N_2O_7P$ phosphonic diacid form
$C_{14}H_{27}N_3O_7P$ triethylammonium salt
$MW_{diacid\ form}$ = 280.18 g.mol^{-1}
$MW_{ammonium\ salt}$ = 380.37 g.mol^{-1}
Ammonium salt is a colorless oil (60 mg, 32 %)



II.16. (±)-2-(5-Methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonic acid 5b

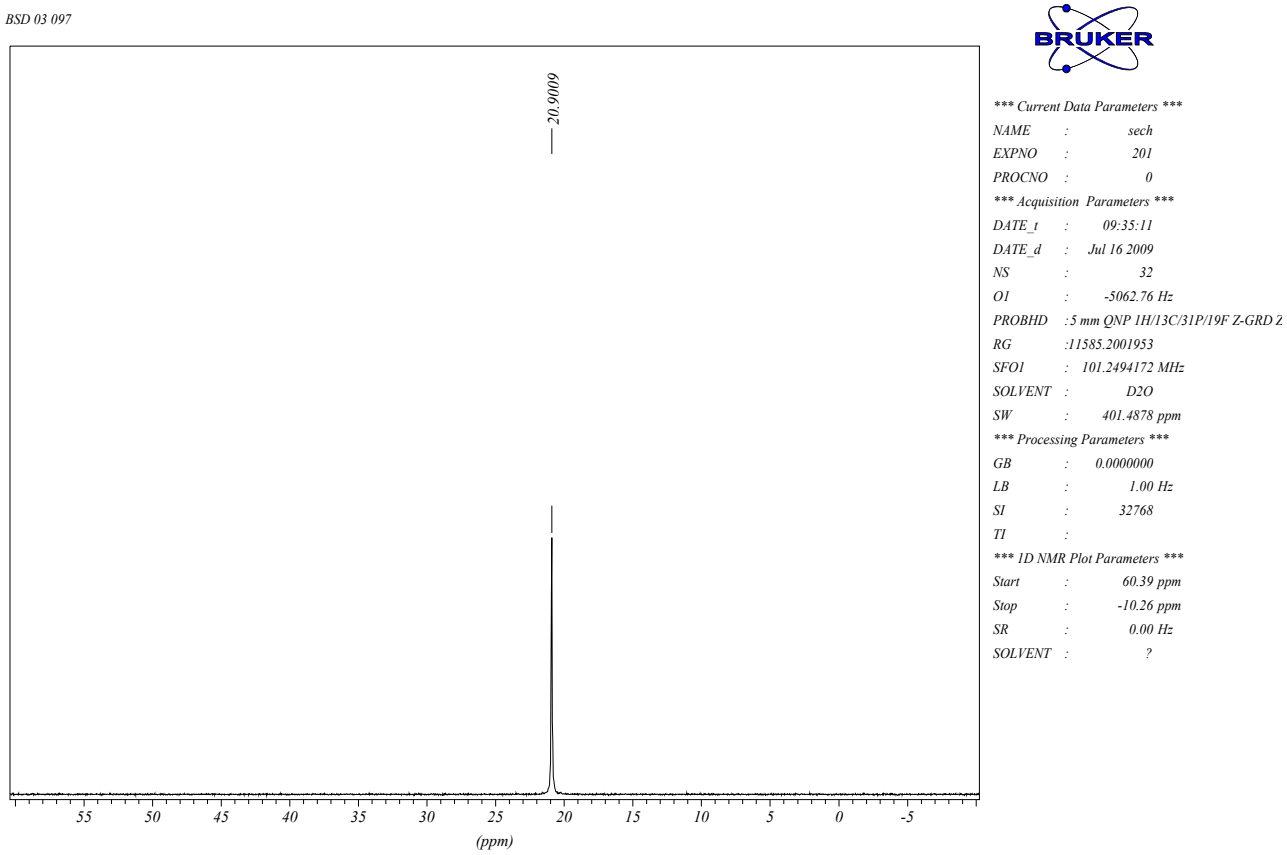


Scheme 4 Synthesis of free phosphonic acid and mono-lithium salt derivatives **5a**-c and **12a-c**

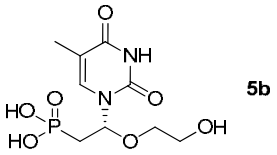


5b

$C_9H_{15}N_2O_7P$
MM = 294.20 g.mol^{-1}
White solid (116 mg, 74%)

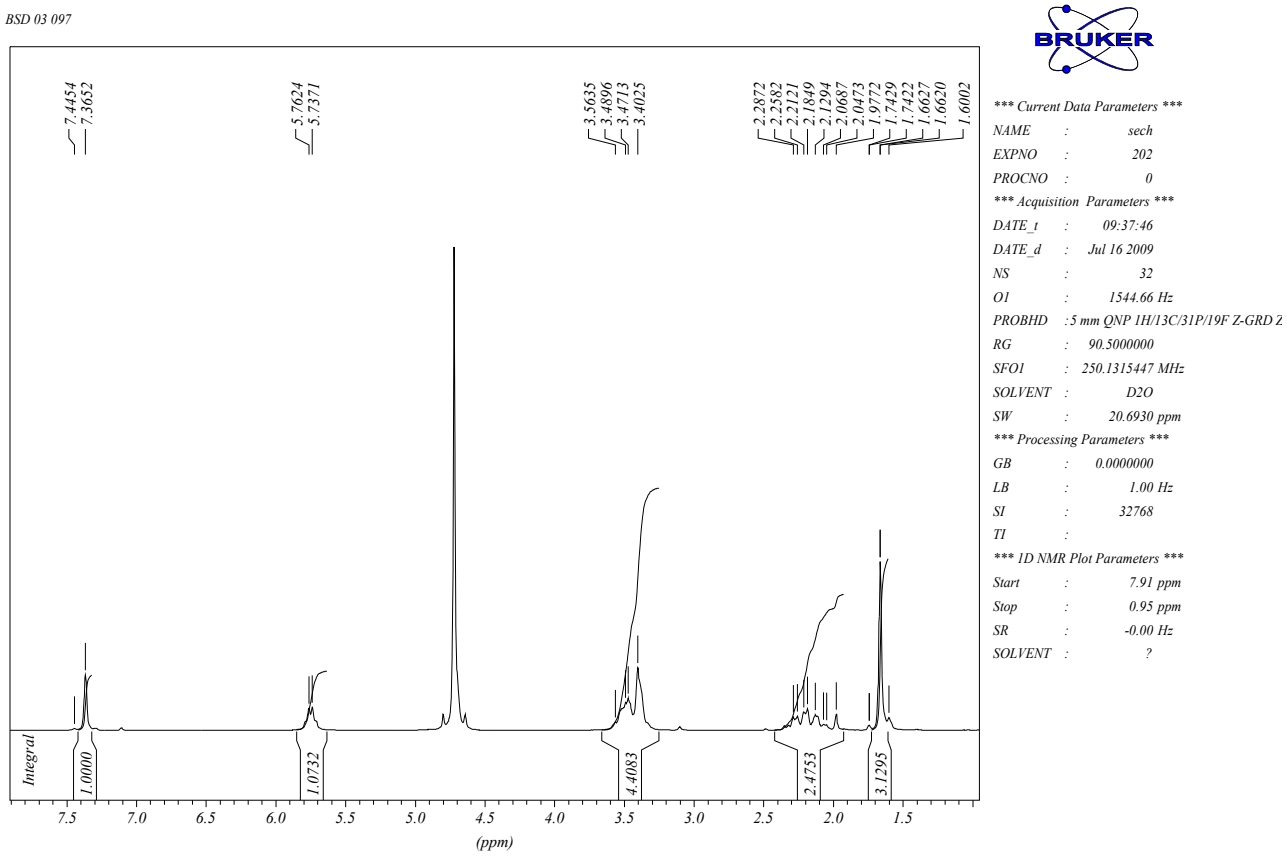


(±)-2-(5-Methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonic acid 5b

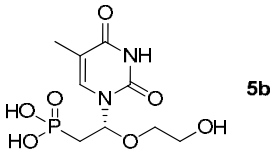


5b

$C_9H_{15}N_2O_7P$
MM = 294.20 g.mol^{-1}
White solid (116 mg, 74%)

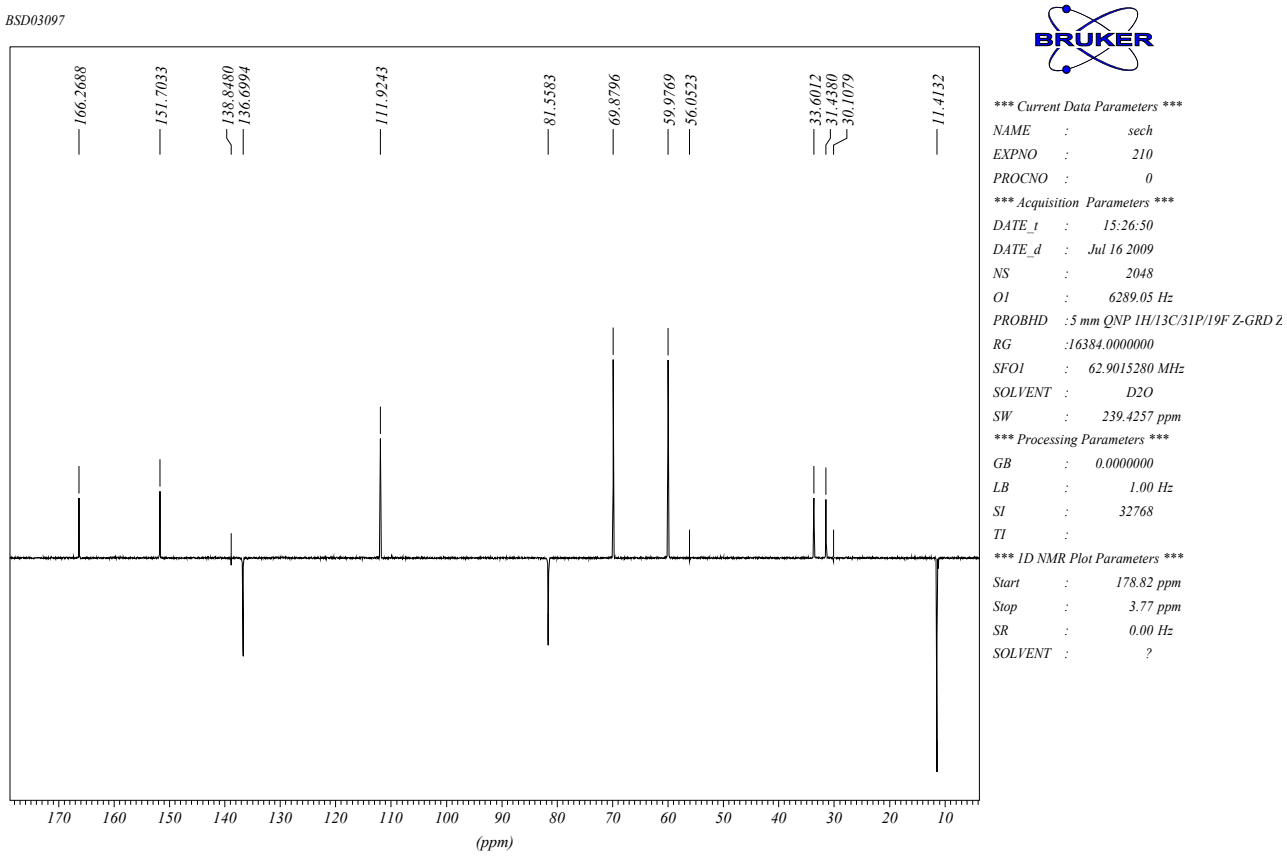


(±)-2-(5-Methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonic acid 5b

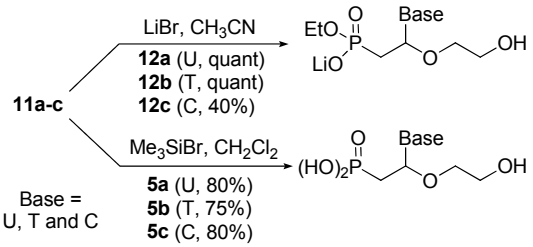


5b

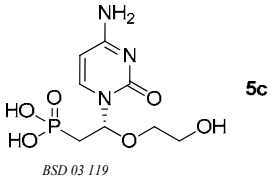
$C_9H_{15}N_2O_7P$
MM = 294.20 g.mol^{-1}
White solid (116 mg, 74%)



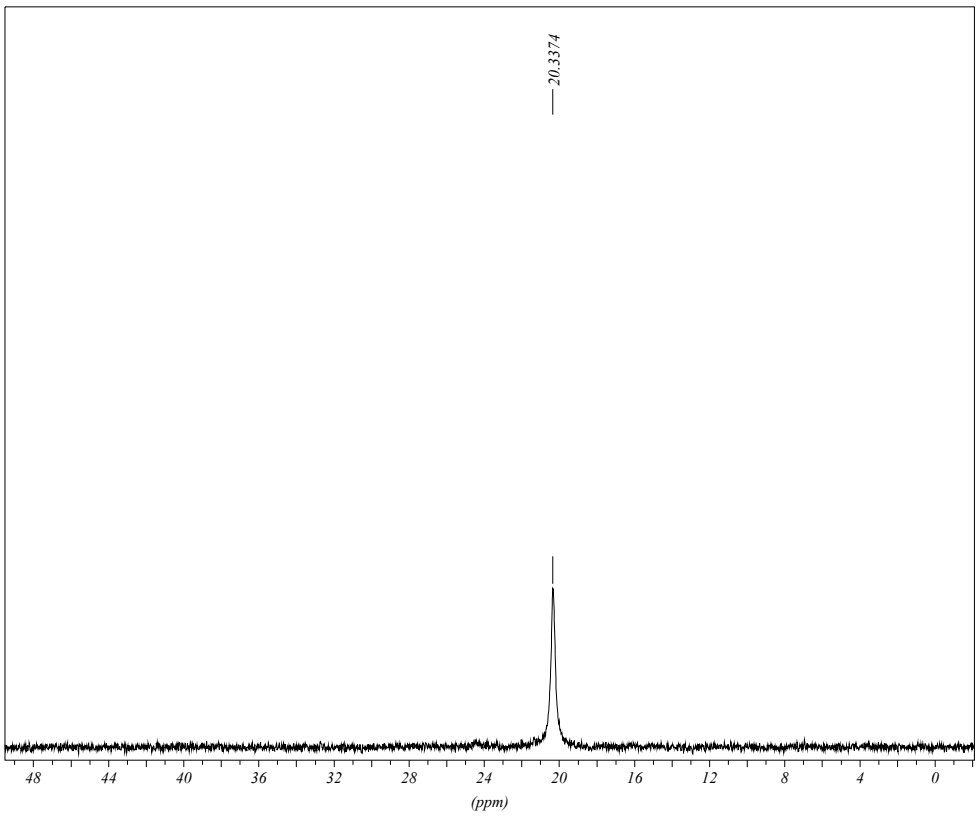
II.17. (±)-2-(4-Amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonic acid 5c



Scheme 4 Synthesis of free phosphonic acid and mono-lithium salt derivatives **5a**-c and **12a-c**

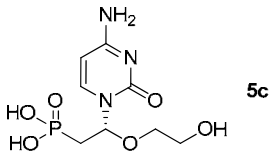


$C_8H_{14}N_3O_6P$
MW = 279.19 g.mol^{-1}
Colorless oil (81 mg, 97%)



*** Current Data Parameters ***
NAME : 119
EXPNO : 202
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 01:49:45
DATE_d : Jul 17 2009
NS : 16
O1 : -5062.76 Hz
PROBHD : 5 mm QNP 1H/13C/31P/19F Z-GRD Z
RG : 8192.0000000
SFO1 : 101.2494172 MHz
SOLVENT : D2O
SW : 401.4878 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 49.52 ppm
Stop : -2.11 ppm
SR : 0.00 Hz
SOLVENT : ?

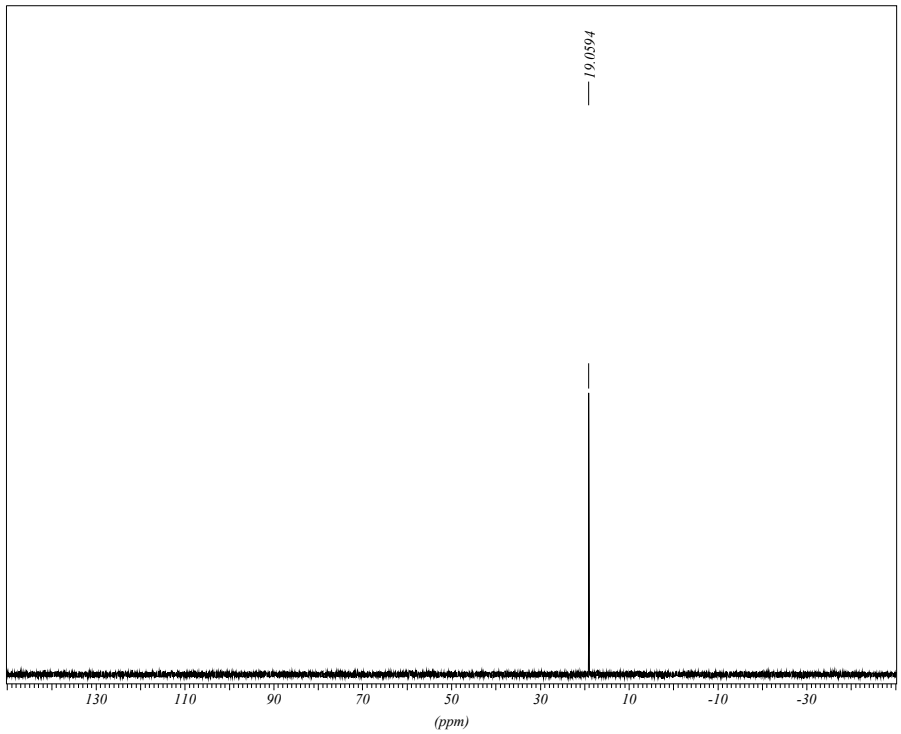
(±)-2-(4-Amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonic acid 5c



5c

$C_8H_{14}N_3O_6P$
MW = 279.19 g.mol^{-1}
Colorless oil (81 mg, 97%)
Triethylammonium salt

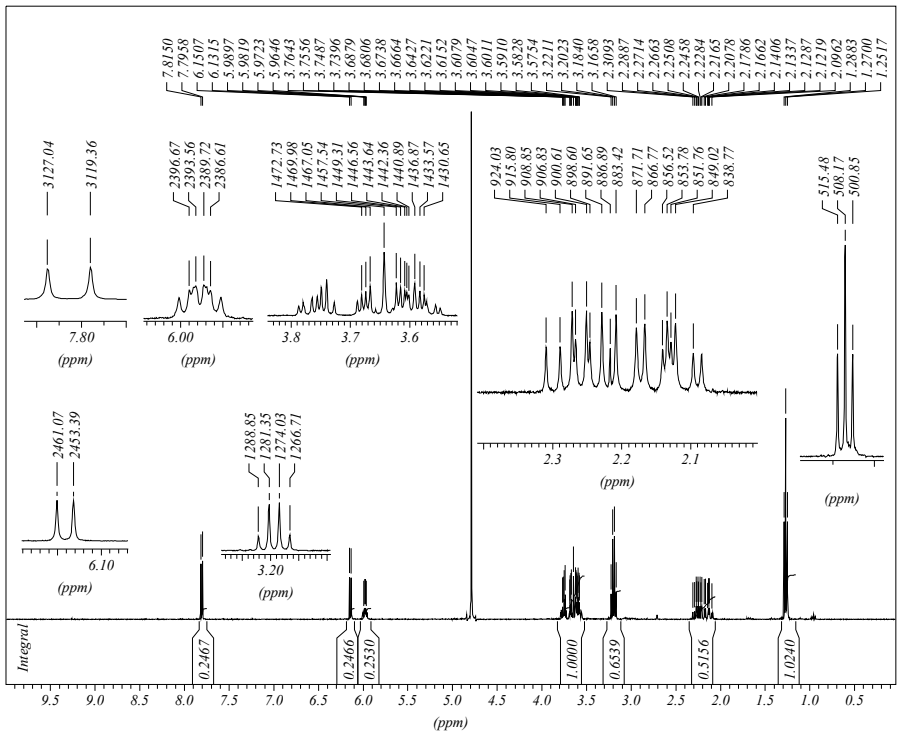
BSD 04 069 F1P31CPD CDCl3 opt/topspin cristau 58



BRUKER

*** Current Data Parameters ***
NAME : t9
EXPNO : 210
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 08:29:58
DATE_d : Jan 18 2010
DE : 8.0 usec
DS : 4
NS : 16
NUC1 : 31P
O1 : 8098.78 Hz
O2 : 1600.52 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-GRD Z840
RG : 20642.5000000
SFO1 : 161.9836718 MHz
SW : 200.4371 ppm
SW_h : 32467.532 Hz
TD : 65536
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
PC : 1.40
SF : 161.9755730 MHz
*** 1D NMR Plot Parameters ***
Start : 150.22 ppm
Stop : -50.22 ppm
SR : 0.01 Hz
ppm_cm : 9.50
Hz_cm : 1538.75

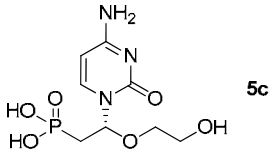
BSD 04 069 F1PROTON CDCl3 opt/topspin cristau 58



BRUKER

*** Current Data Parameters ***
NAME : t9
EXPNO : 211
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 08:33:27
DATE_d : Jan 18 2010
DE : 8.0 usec
DS : 2
NS : 16
NUC1 : 1H
O1 : 2400.78 Hz
O2 : 2470.97 Hz
PROBHD : 5 mm PAQNP Switch-1H Z-GRD Z840
RG : 406.3999939
SFO1 : 400.1324008 MHz
SW : 14.9831 ppm
SW_h : 5995.204 Hz
TD : 65536
*** Processing Parameters ***
GB : 0.0000000
LB : 0.10 Hz
PC : 1.00
SF : 400.1309810 MHz
*** 1D NMR Plot Parameters ***
Start : 10.00 ppm
Stop : 0.04 ppm
SR : 981.48 Hz
ppm_cm : 0.47
Hz_cm : 188.87

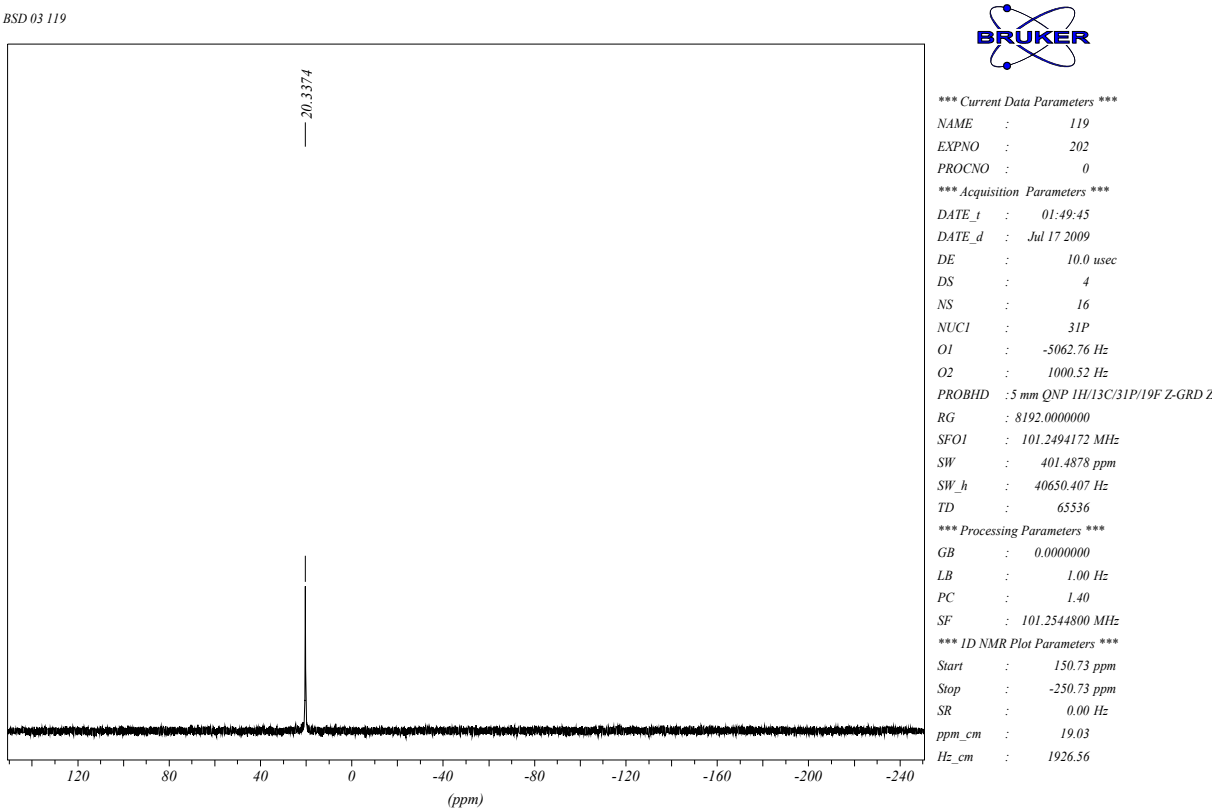
(±)-2-(4-Amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonic acid 5c



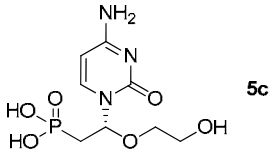
5c

Acidic form

$C_8H_{14}N_3O_6P$
MW = 279.19 g.mol^{-1}
Colorless oil (81 mg, 97%)



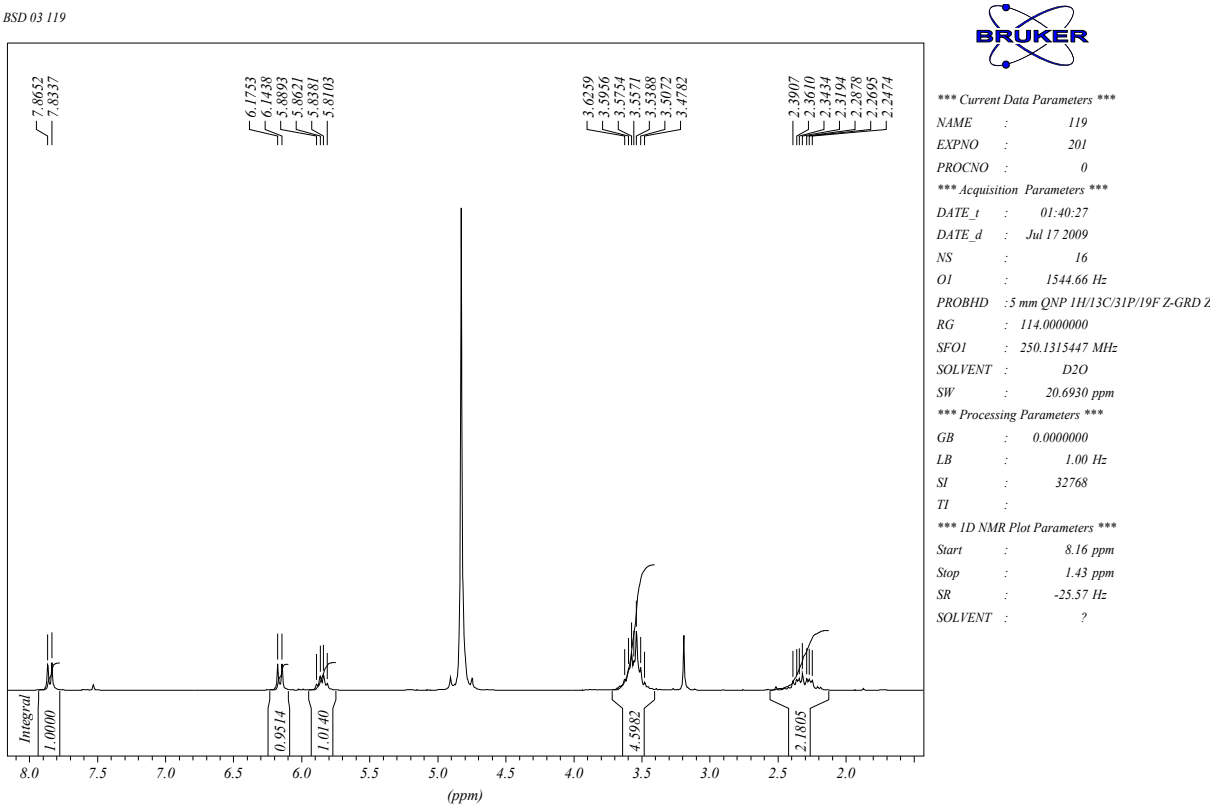
(±)-2-(4-Amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonic acid 5c



5c

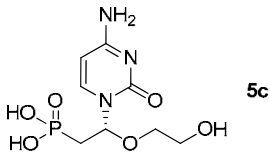
$C_8H_{14}N_3O_6P$
MW = 279.19 g.mol^{-1}
Colorless oil (81 mg, 97%)

Acidic form



*** Current Data Parameters ***
NAME : 119
EXPNO : 201
PROCNO : 0
*** Acquisition Parameters ***
DATE_t : 01:40:27
DATE_d : Jul 17 2009
NS : 16
O1 : 1544.66 Hz
PROBHD : 5 mm QNP 1H/13C/31P/19F Z-GRD 2
RG : 114.0000000
SFO1 : 250.1315447 MHz
SOLVENT : D2O
SW : 20.6930 ppm
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
Start : 8.16 ppm
Stop : 1.43 ppm
SR : -25.57 Hz
SOLVENT : ?

(±)-2-(4-Amino-2-oxo-2H-pyrimidin-1-yl)-2-(2-hydroxyethoxy)ethylphosphonic acid 5c



5c

$C_8H_{14}N_3O_6P$
MW = 279.19 g.mol^{-1}
Colorless oil (81 mg, 97%)

Acidic form